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Contents on Inside Cover

American Heart Journal

For the Study of the Circulation

CONTENTS FOR JULY, 1946

Original Communications

Clinical Reports

Abstracts and Reviews

Announcements

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American Heart Journal

VOL. 32 JULY, 1946 NO. 1

Original Communications

FOREIGN BODIES IN AND IN RELATION TO THE THORACIC BLOOD VESSELS AND HEART

III. INDICATIONS FOR THE REMOVAL OF INTRACARDIAC FOREIGN BODIES AND THE BEHAVIOR OF THE HEART DURING MANIPULATION

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ARMY OF THE UNITED STATES

ARISTOTLE wrote, "The heart alone of all viscera cannot withstand serious injury."[1] At the end of the last century, Stephen Paget[2] had gained no optimism, for he commented, "Surgery of the heart has probably reached the limit set by Nature to all surgery: no new method, and no new discovery, can overcome the natural difficulties that attend a wound of the heart," yet less than one year later, on Sept. 9, 1896, Rehn,[3] in Frankfurt, successfully sutured a stab wound of the right ventricle. Within ten years over a hundred such cases of cardiac suture had been reported, and now several hundred more have been added, the majority of which have been successful.

Elective intracardiac surgery first centered around the removal of foreign bodies. Decker[4] reported that there had been at least twenty-four successful cases by 1939. There will be more when the results of surgery in World War II are known.

The brilliant work and writing on heart surgery by Doyan, Duval, Tuffier, Carrel, Graham, Beck, and Cutler mark the evolution from dreams to experiment and from experiment to bold human adventure.

Today it is fair to expect certain simple intracardiac maneuvers to be successful. The door has been opened by modern anesthesia and the technique of rapid blood replacement.

The purpose of this paper is twofold: first, *to elaborate on the indications for surgical removal of intracardiac foreign bodies;* and second, *to describe and*

Appreciation is expressed to the Sias Laboratories of the Brooks Hospital, Brookline, Mass., for their assistance in the publication of this article and for the provision of facilities for further investigation in cardiac surgery now being undertaken.

Presented as the substance of the Joseph Strickland Goodall Memorial Lecture at the Society of Apothecaries, London, on June 26, 1945.

Received for publication Sept. 21, 1945.

illustrate the behavior of the heart during manipulation. The discussion is based on experience in the removal of missiles distributed as indicated in Table I, and is concerned principally with the 26 pericardial and 13 intracardiac missiles. Fig. 1 shows the intracardiac missiles that have been removed. There are seven from the chamber of the right ventricle, four from the chamber of the right auricle, one from the left auricular cavity, and one from a small cystic myocardial hernia in the left ventricle.

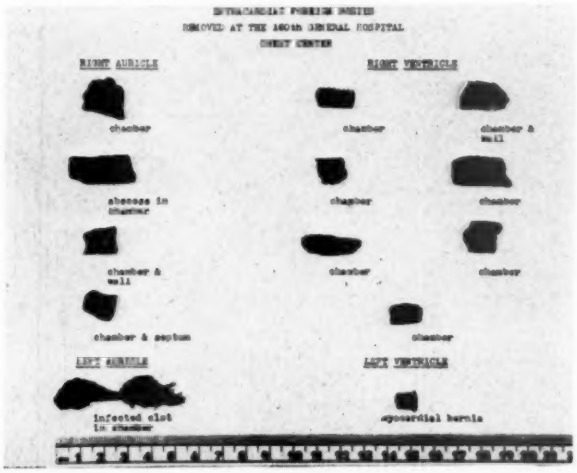


Fig. 1.—Intracardiac foreign bodies that have been removed.

TABLE I. DISTRIBUTION OF 134 MISSILES IN RELATION TO THE PERICARDIUM, HEART, AND GREAT VESSELS

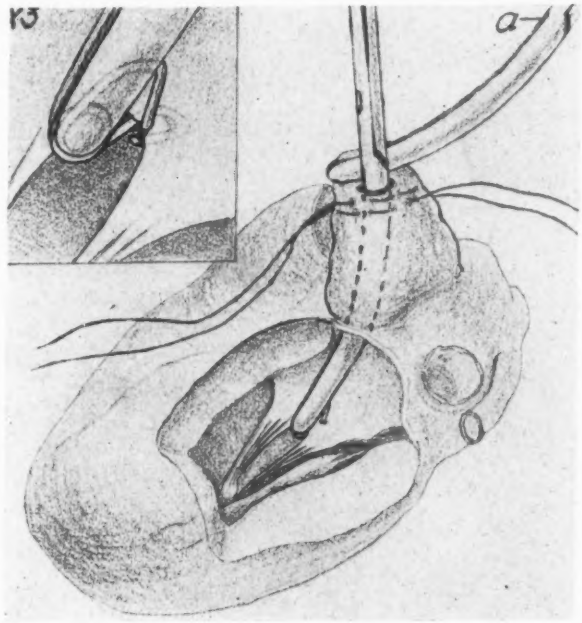
Pericardial	26
Involving pericardium but principally pulmonary	17
Intracardiac	13
On great vessels (and in walls)	35
Intravascular (three embolic)	7
On great vessels but principally pulmonary	17
Mediastinal but not directly on great vessels	19
Total	134
Deaths	0

INDICATIONS FOR REMOVAL OF INTRACARDIAC FOREIGN BODIES

The first part of this discussion pertains to the indications for the removal of intracardiac foreign bodies.

The pressure of work during the past year has been such that there was little time for review of the medical literature. When such consultation was sought it was usually disappointing. Often it has been difficult to accept reported foreign bodies as "*in the heart*" when there has been no confirmation of the location by autopsy or surgical exploration. Even surgical exploration may be uncertain in the presence of an infected hematoma within the pericardium or auricle. In short, it is probable that some of the reported "intracardiac" missiles were not *in the heart.*

Personal experience confirmed the difficulty of accurate localization of metallic fragments in relation to the heart. Almost one-half of the foreign bodies referred to us as "in the heart" were found by careful fluoroscopic examination to lie outside it. Furthermore, one-third of the cases that we thought earlier in our work might represent intracardiac fragments were found at operation to be extracardiac.



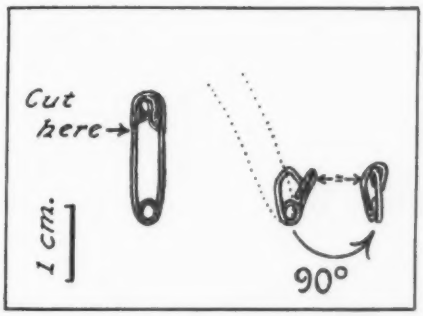


Fig. 2.—Method of implantation of a foreign body in the heart of a dog.

Such confusion makes it very difficult to assess the risks to health and life of intracardiac missiles. During the past year, however, these problems arose, and it was necessary to establish a working policy. This policy was formulated from information borrowed from the medical literature, from our own hypothetical concepts, and from a limited amount of previous experimental work on animals.

It was felt that certain cardiac foreign bodies should be removed, for the following reasons: (1) to prevent embolus of the foreign body or associated thrombus, (2) to reduce the danger of bacterial endocarditis, (3) to prevent recurrent pericardial effusions, and (4) to diminish the incidence of myocardial damage.

For these reasons it was decided to remove half of the missiles presumed to be in the heart that came under our observation. Applicability of these factors was determined, in part, by the size and location of the foreign body and by clinical manifestations. Clinical evidence supporting these tenets has accumulated during the year.

The first and most obvious indication for removal is the *prevention of embolus of the foreign body or of an associated thrombus.* Several instances of this accident have been recorded in the literature and two additional cases may be briefly noted here.

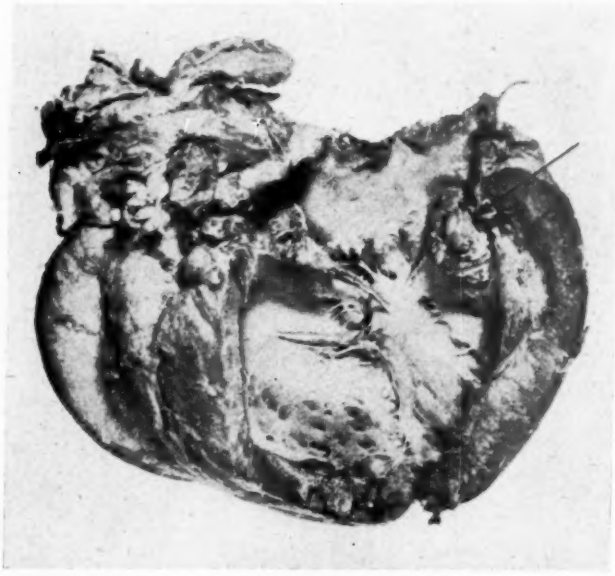


Fig. 3.—Typical endocarditis surrounding the implanted foreign body.

One of our patients developed, shortly after injury, a hemiplegia coming from a thrombus in the left auricle. The foreign body lay in the interauricular septum and right auricle. It was removed from the right auricle.[5]

A second and particularly significant case has recently been described by Lieutenant Colonel Nichol.[6] In this instance the missile was in the left ventricle. Embolism causing hemiplegia occurred over two weeks after injury.

The second tenet, that certain foreign bodies should be removed *to reduce the danger of bacterial endocarditis,* was based in part on experimental work with dogs.[7] Foreign bodies were placed in various locations in the heart, and bacterial endocarditis developed spontaneously. Fig. 2 shows the manner of

implantation and the type of foreign body used. Figs. 3 and 4 illustrate typical resultant bacterial valvulitis and septic embolic infarcts. It was feared that foreign bodies might behave in the same way in human hearts.

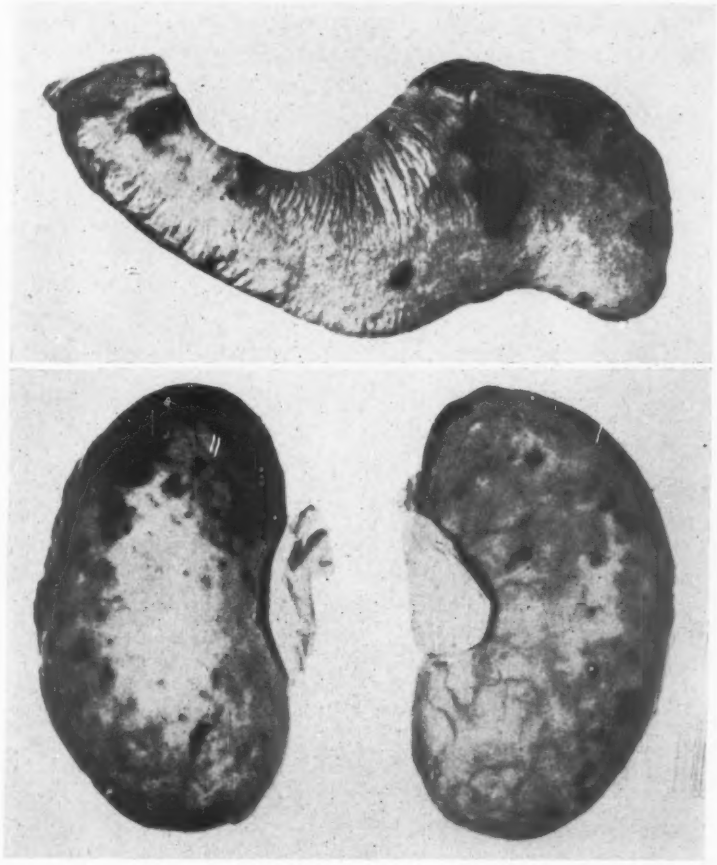


Fig. 4.—Typical septic embolic infarcts of experimental bacterial endocarditis.

Our clinical support for this indication is not complete. One patient ran a course suggesting subacute bacterial endocarditis with spiking fever, tachycardia, and an acute episode of right upper quadrant pain with jaundice. Response to surgical removal of the missile and its associated thrombus from the right auricle was immediate and dramatic, with prompt recovery from an almost moribund state. Furthermore, in bacteriologic studies of four intra-auricular foreign bodies, pathogenic organisms grew from three of these foreign bodies. One of these lay in a small abscess in the center of a mural thrombus in the right auricle. Similar studies in five right intraventricular fragments showed growth of bacteria in only one instance; here also the foreign body lay in an abscess within a mural thrombus in the chamber of the right ventricle. No bacteriologic studies are available on the four other cases.

It cannot be said that these infected niduses represent true bacterial endocarditis nor that they would have produced it. Nevertheless, these findings have encouraged us to remove the missiles.

The third reason for the removal of missiles is to *prevent recurrent pericardial effusions.* This point has been stressed in the medical literature. We have seen two such cases, but the symptoms were not severe enough nor were the fragments of sufficient size to justify intervention. Size and clinical manifestations will inevitably govern surgical removal of cardiac missiles. Fig 1 shows those that we have removed. We have elected to leave more than we have removed; the former were, of course, both small and silent.

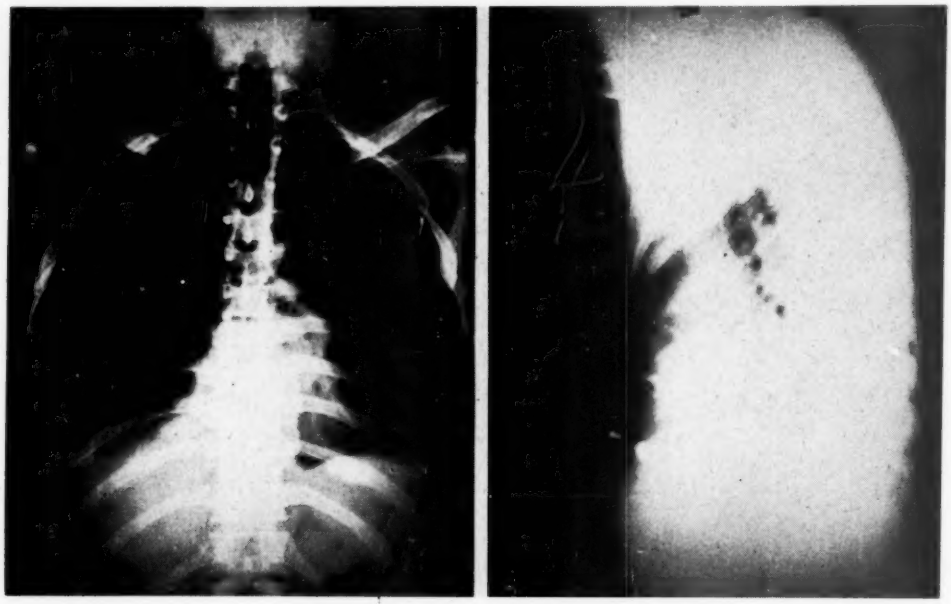


Fig. 5.—Posteroanterior and lateral roentgenograms demonstrating the original position of the fragment in the right ventricle.

Finally, cardiac missiles should be removed to *diminish the incidence of myocardial damage.*

Damage of the right ventricular wall overlying the site of a migratory missile has been noted in one instance. This case is presented in some detail, for it is of special significance in several respects. In particular it demonstrates clearly that a foreign body, simply lying in the chamber of the heart, can produce considerable damage of the overlying myocardium in three months. This case further indicates that operative removal per se need not cause significant myocardial injury.

LeR. R., a 29-year-old infantry sergeant was struck by a mortar shell fragment in the right lower posterior aspect of his chest on July 21, 1944, near St. Lo, France. Fluoroscopy and roentgenograms (Fig. 5) showed a metallic foreign body pulsating with the heart, lying in the anterior portion

of the right ventricle, just to the left of the midline. An electrocardiogram on July 25 (Fig. 6) showed only inverted T waves in the right-sided precordial leads CF_1, CF_2, and CF_3. By August 8 the T wave in CF_3 had become upright, so that the tracing appeared normal.

At operation on August 15, the missile was grasped through an incision in the right ventricle, only to be pulled from the forceps by the wriggling myocardium and to be lost from sight and palpation, in the blood stream. The technical details of cardiotomy have been presented elsewhere.[5]

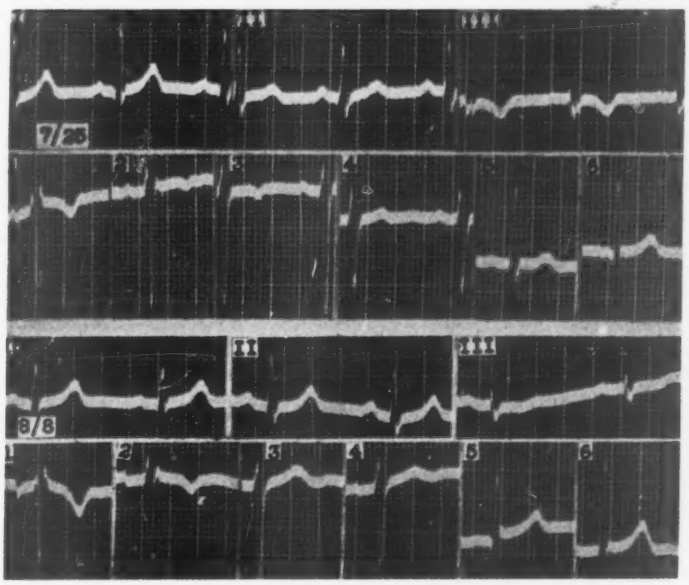


Fig. 6.—Electrocardiograms before the first cardiotomy. The figures in the upper left corner of each segment indicate the leads (Roman numerals for the limb leads and Arabic numerals for the precordial leads CF_1 to CF_6). The date of tracing appears in lower margin of the section.

After operation, the foreign body was found by roentgenograms (Fig. 7) to be in the right auricle over the opening of the inferior vena cava. On August 17 the electrocardiogram (Fig. 8) showed elevated S-T segments in Leads I and II, which fell by September 1. Later the T waves also became sharply inverted in Leads I and II and in the left-sided precordial leads CF_4, CF_5, and CF_6. This pattern suggests acute anterior wall myocardial damage and may be related to the incision made in the right ventricle near the septum in the anterior surface of the heart, or to the associated pericarditis.

At a second cardiotomy on Nov. 16, 1944 (three months later), the missile was visualized and palpated in the right auricle just above the entrance of the inferior vena cava. It escaped again, however, and fell back into the right ventricle to the position seen in the postoperative roentgenogram (Fig 9). A significant point is demonstrated by these roentgenograms; that the imperfect lateral position gives the impression that the missile is in the chest wall. Electrocardiograms (Fig. 10) showed no specific acute change following this second

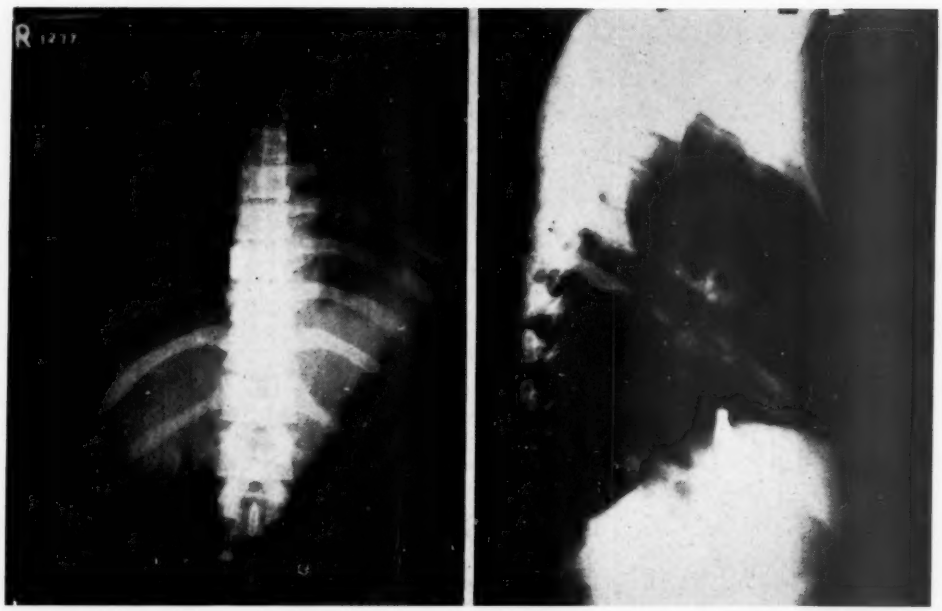


Fig. 7.—Posteroanterior and lateral roentgenograms showing the position of the fragment in the right auricle after the first cardiotomy.

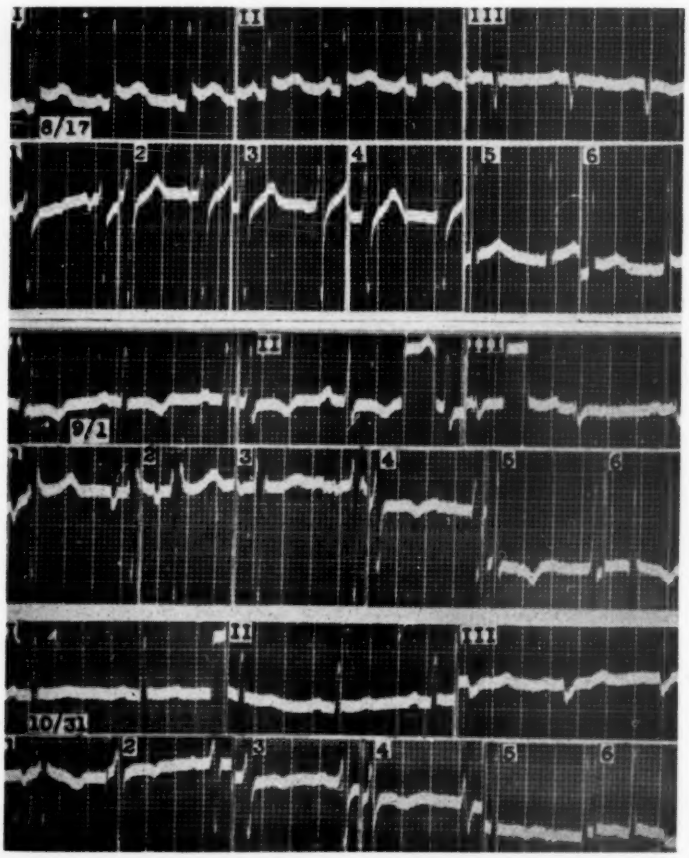


Fig. 8.—Electrocardiograms taken after the first cardiotomy.

cardiotomy, but only a progressive return toward normal of the T waves in Leads I, II, CF_5, and CF_6.

On Feb. 19, 1945, a third cardiotomy was performed, again through an anterior approach similar to the first operation. The old scar of the first incision in the right ventricle was found to be solidly healed after this interval of six months. Considerable fibrous pericarditis had developed but it did not limit cardiac motion nor obstruct blood flow. Near the apex of the right ventricle,

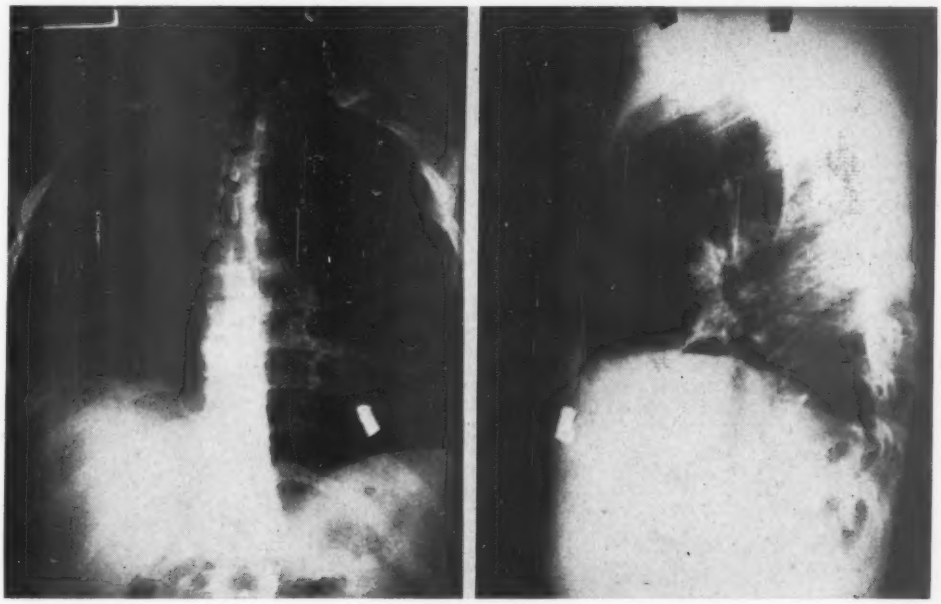


Fig. 9.—Posteroanterior and lateral roentgenograms of the fragment again in the right ventricle after the second unsuccessful cardiotomy.

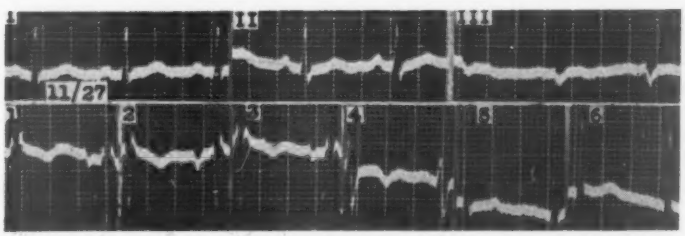


Fig. 10.—Electrocardiogram taken after the second cardiotomy.

however, the muscle wall was thin, flabby, and discolored; the foreign body was palpable in the underlying right ventricular cavity. This area of myocardial damage had been produced by the muscle wall rubbing over the fragment during the three months following the second operation. The heart was opened again through this flabby area, and the shell fragment (Fig. 1) was grasped by forceps and removed with only moderate difficulty (Plate I). The period of

intracardiac manipulation extended for approximately three minutes, in three episodes. Showers of extrasystoles were noted during the process of removal. The cardiac behavior at this time is recorded in the electrocardiograms (Fig. 11) that are discussed later.

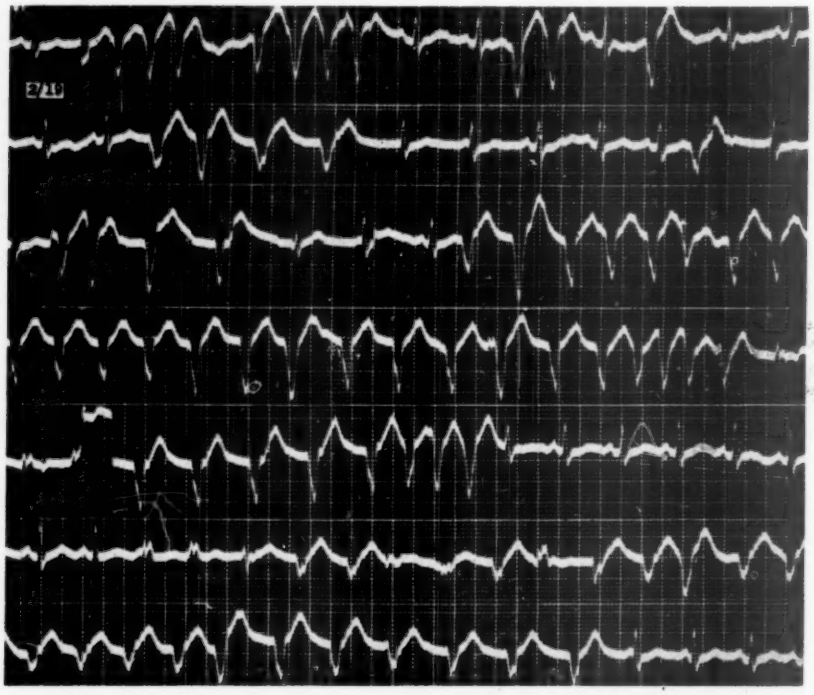


Fig. 11.—Electrocardiographic tracings taken during the successful cardiotomy at the time of removal of the fragment from the right ventricle.

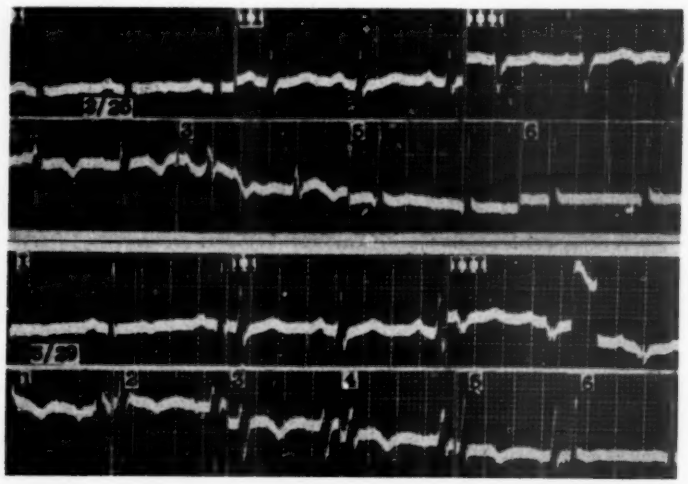


Fig. 12.—Electrocardiograms following the third cardiotomy.

Convalescence following operation was uneventful. Postoperative electrocardiograms (Fig. 12) showed only left axis deviation and low or inverted T waves in Lead I and the precordial leads, findings which were consistent with pericardial reaction and residual minor damage in the mid-precordial area.

Fig. 13 recapitulates the migration of the missile from the right ventricle to the right auricle and back again. Fig. 14 shows the patient clinically well at the time of discharge.

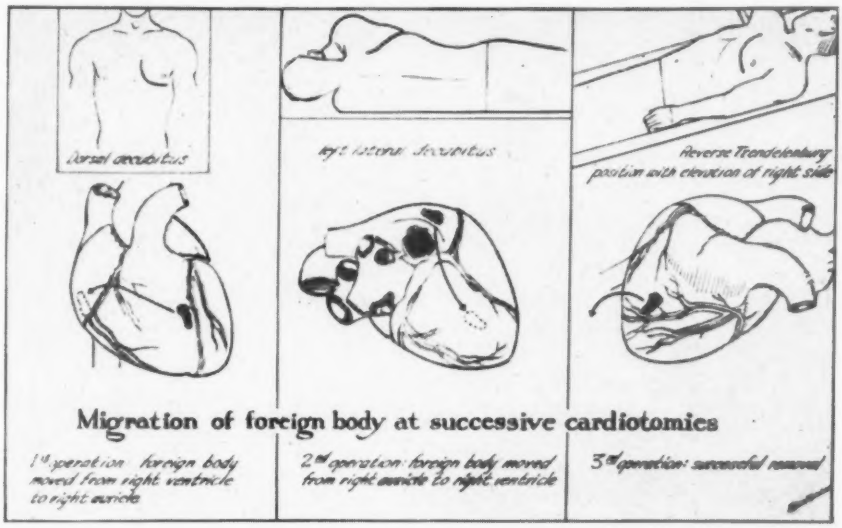


Fig. 13.—Diagrammatic presentation of the patient's position at operations and of the migration of the missile.

In the only case in this series of a foreign body in the left ventricle, the missile lay in a small cystic myocardial hernia (Fig. 15). Roentgenkymographic studies showed diminished amplitude of pulsation at the apex and passive left ventricular dilatation during systole, suggesting early ventricular aneurysm or hernia. Electrocardiograms (Fig. 16) showed a persistent pattern characteristic of extensive damage of the anterior wall of the left ventricle. The changes consisted of low voltage, deep Q_1, absent R_1 and inverted T_1, together with inverted and "W-shaped" QRS complexes and sharply inverted and coved T waves in the left-sided precordial leads.

At operation, the foreign body was found in the left ventricle, in a cystic zone of myocardial damage 1.5 cm. in diameter. It was ballottable in the defect in the cardiac wall, and paradoxical pulsation of this area of the ventricle was noted. The missile (Fig. 1) was removed without hemorrhage because of a mural thrombus. The thrombus was not disturbed. The myocardial defect was closed and reinforced with two superimposed pericardial grafts. It is interesting that electrocardiographic tracings taken frequently during the operation showed no evidence of cardiac irritability at any time, except for a few ventricular extrasystoles during the process of endotracheal intubation.

Direct observation at operation indicated that the danger of rupture of this myocardial hernia was real and was aggravated by the presence of the foreign body. It is thought that this operation in which the missile was removed and the defect was repaired prevented progression of the myocardial damage and possible rupture of the heart.

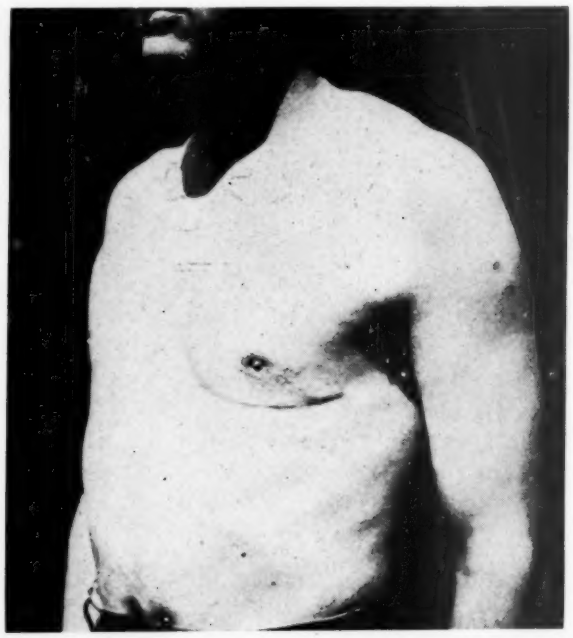


Fig. 14.—Patient LeR. R. at the time of discharge.

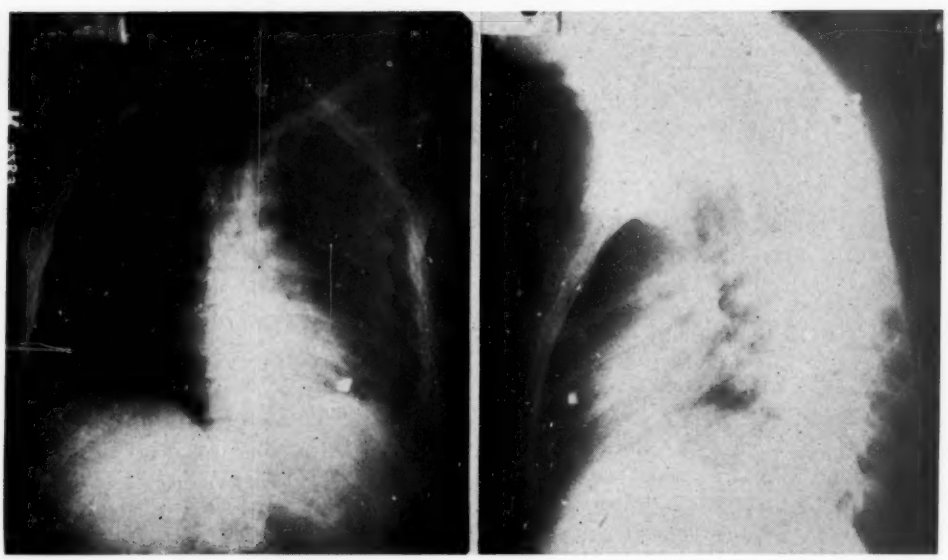


Fig. 15.—Posteroanterior and lateral roentgenograms of a missile in the left ventricle.

A third patient was seen by Major Fred Jarvis.[8] In this case, the wall of the right ventricle overlying a migratory missile degenerated and death ensued.

A fourth case, this from our own series, seems particularly significant in that it demonstrates in combination several of the tenents under discussion.

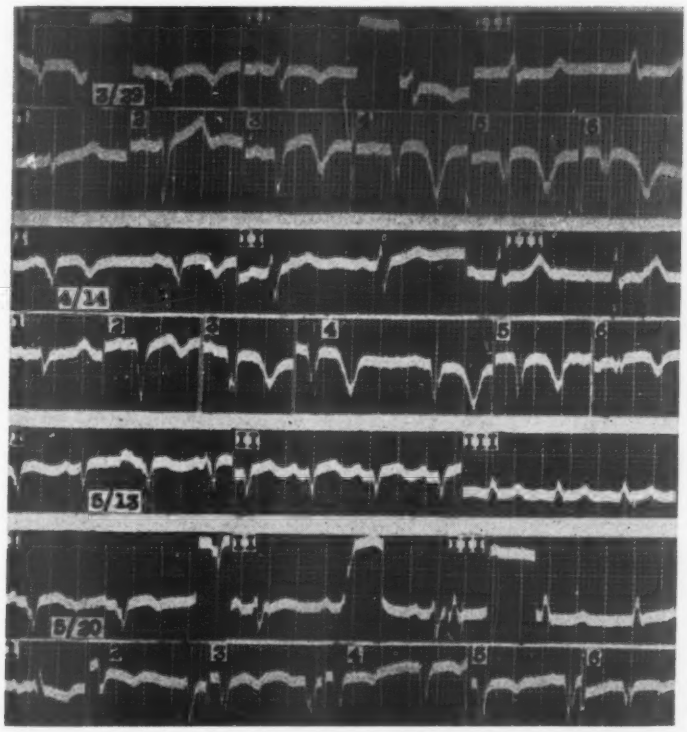


Fig. 16.—Electrocardiograms showing left ventricular damage.

This soldier developed an empyema (hemolytic *Staphylococcus aureus* and *Clostridium welchii*) following injury by a shell fragment in the left anterior aspect of the chest. The empyema was treated by decortication and, later, by open drainage before he arrived at the 160th General Hospital Chest Center. Three massive and two minor episodes of hemorrhage occurred in the six months following injury; there were also bouts of pyrexia reaching 103° F. that did not appear to be due to the empyema. Fig. 17 shows the size and location of the foreign body, and Fig. 18 presents typical electrocardiographic tracings. Before operation there were right axis deviation with low R_1 and deep S_1, low diphasic T_1, and upright pointed T_2 and T_3. The precordial leads were normal. These findings did not help in localization of the missile.

At operation on May 18, 1945, the empyema was found to communicate with a laceration in the pericardium and underlying adherent left auricle. There was a laceration of the auricle that was plugged by a large infected intracardiac hematoma. The 2 by 1 by 1 cm. missile was wrapped in cloth and lay

in this clot. The fragment was removed from the left auricle together with the cloth and the infected clot. *Cl. welchii* and *Escherichia coli* were grown on direct culture of the foreign body. The surgical exposure, location of the pericardial laceration, and type of repair are described elsewhere.[5]

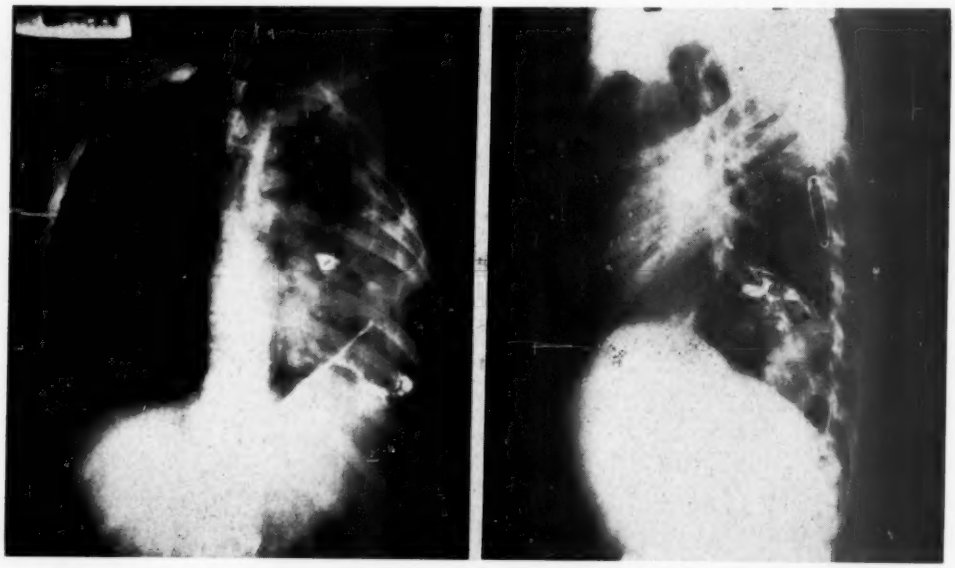


Fig. 17.—Posteroanterior and lateral roentgenograms of a fragment in the left auricle. Radio-opaque oil is seen in the empyema pocket.

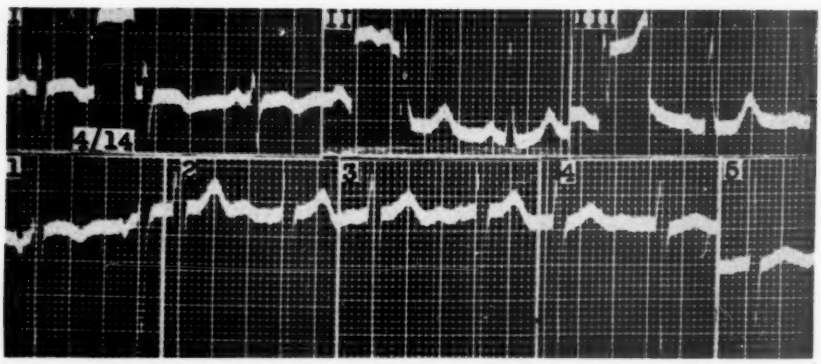


Fig. 18.—Electrocardiograms before operation in the patient with left auricular laceration and an intra-auricular shell fragment.

After operation there was rapid improvement of the empyema, and no further episodes of hemorrhage or pyrexia occurred. Electrocardiograms (Fig. 19) show deep and sharp inversion of T_1 and inverted T waves in CF_5, but no other significant change. This case appeared to embrace most of the indications for removal of an intracardiac foreign body: extensive thrombus with potential embolus, gross intracardiac contamination and infection, pericardial involvement, and damaged myocardium with repeated hemorrhage.

Two additional factors may assume importance in the decision to remove intracardiac foreign bodies: namely, *pain and cardiac neurosis.*

Pain has been associated with some of the pericardial missiles but with only one of the intracardiac group. This was in a man in whom the missile had migrated from the auricle to the ventricle. A similar case is described by Lieutenant Colonel Miscall.[9]

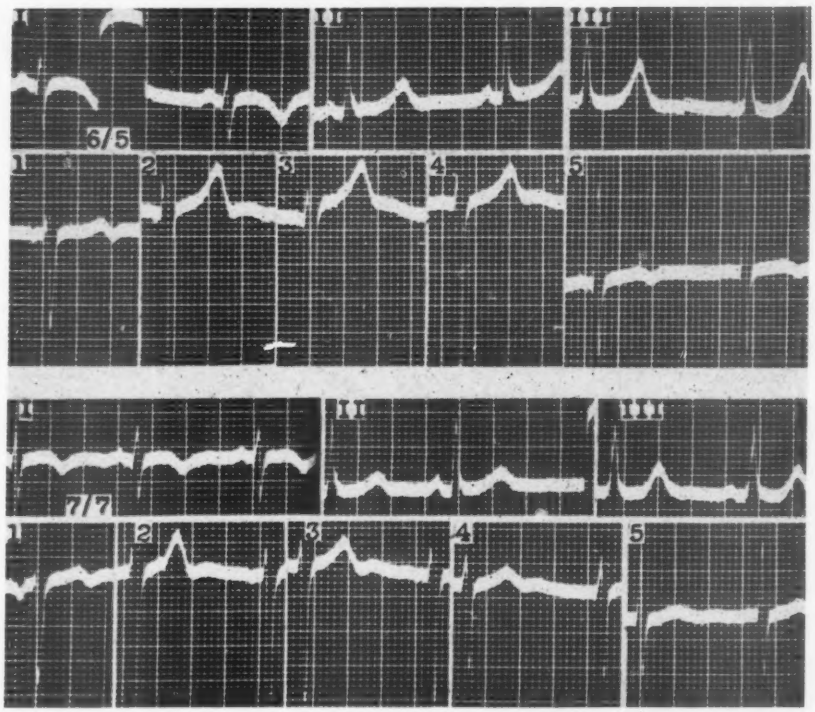


Fig. 19.—Electrocardiograms following left auricular cardiotomy.

Cardiac neurosis may become an important consideration in spite of every effort to reassure the patient. All our patients with foreign bodies in or near their hearts have wanted them removed. Professor Grey Turner has said: "In addition to the characteristic cardiac symptoms just mentioned, there may be neurotic manifestations which mainly depend on the attitude of the patient to the knowledge that he harbors a foreign body in one of the citadels of his wellbeing."[10]

These are fragments of clinical evidence directing the surgeon to remove the larger or symptomatic missiles. The experience has been brief, yet convincing to us. It is emphasized that we decided to leave fifteen fragments in the heart. These, of course, were small and silent. Surgery was undertaken in four additional cases where intracardiac fragments were present. Two of these fragments were deemed too hazardous to remove at exploratory *pericardiotomy,* and two were not recovered at *cardiotomy.*

The cost of operation to the patients has not been great; none died; all have done well and apparently have normally functioning hearts now. Final conclusions cannot be drawn for several years.

BEHAVIOR OF THE HEART DURING MANIPULATION

The technique used in approaching and removing cardiac and mediastinal foreign bodies cannot be discussed here. During this experience, however, some elementary rules of surgical conduct governing exposure and manipulation of the heart have become clear. Some salient features of cardiac exposure are the following:

1. *Adequate direct exposure of the involved region.* This requires the use of a variety of approaches.

2. *The conservation of the skeleton of the thoracic cage.* Bone and cartilage may be divided but not removed. After operation there should be neither deformity nor defect.

3. *Minimal dislocation of heart from the position of optimal function.*

4. *Maintenance of moist epicardium in the exposed heart.* One per cent novocaine solution has been used; it may have additional advantages in reducing cardiac irritability.

It is with the third principle of exposure that the remainder of this discussion is to deal; namely, maneuvers that are not tolerated well by the heart during intracardiac and pericardial surgery. One case of an extracardiac and one case of an intracardiac operation will be used as illustrations.

The first demonstrates the effect of dislocation of the heart from the position of optimal function during the removal of an extracardiac foreign body that lay in a pericardial abscess well back on the diaphragmatic surface. The location of the pericardial missile can be seen in the roentgenograms in Fig. 20. At operation the foreign body was found on the posterior phrenic surface of the heart in a pericardial abscess containing about 18 c.c. of pus. To gain access to this area the heart had to be lifted out of the pericardial sac (Plate II). Because this procedure caused fall in blood pressure and circulatory failure, the heart had to be replaced frequently for rest and return of blood pressure toward normal after relatively short periods of dislocation. Many irregularities in rhythm that were apparently extrasystoles occurred. Also, a marked cardiac dilatation, particularly of the right ventricle, developed, with the result that the heart became too large for the pericardial sac (Plate III).

Electrocardiographic tracings taken during operation (Fig. 21) showed variations in rhythm consisting of ventricular extrasystoles (at 300), wandering pacemaker (varying P-R interval at 302 and 307), and A-V nodal rhythm (at 313, 315, and 316). It was at the time that the nodal rhythm occurred that a particularly prolonged and alarming episode of circulatory failure developed during a period of dislocation of the heart; after recovery, normal sinoauricular tachycardia returned (at 317, 319, and 332) (Fig. 21).

An additional change in the electrocardiogram was also related to dislocation of the heart. At 257 the S wave became broad and notched and the QRS

Plate II.

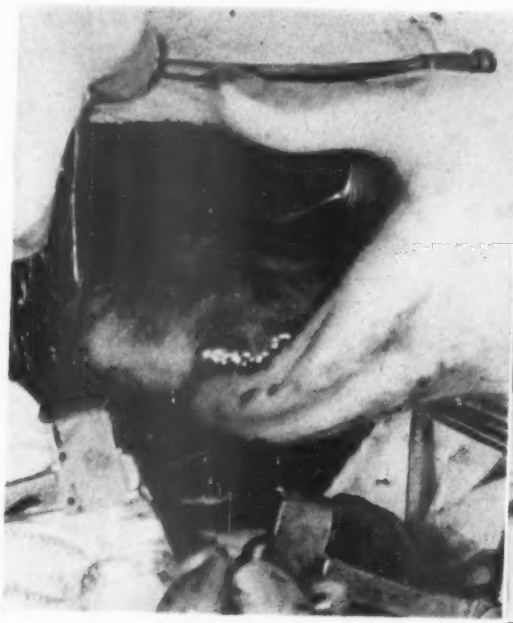


Plate III.

Plate I.—Colored photograph at the instant of incision into the right ventricle. This is the third cardiotomy in Fig. 13.

Plate II.—Colored photograph illustrating the maneuver of dislocation of the heart from the pericardial sac.

Plate III.—Colored photograph showing marked right ventricular dilatation following dislocation of the heart. Plates II and III were taken during the operation recorded in the electrocardiographic tracings in Fig. 21.

Plate I.

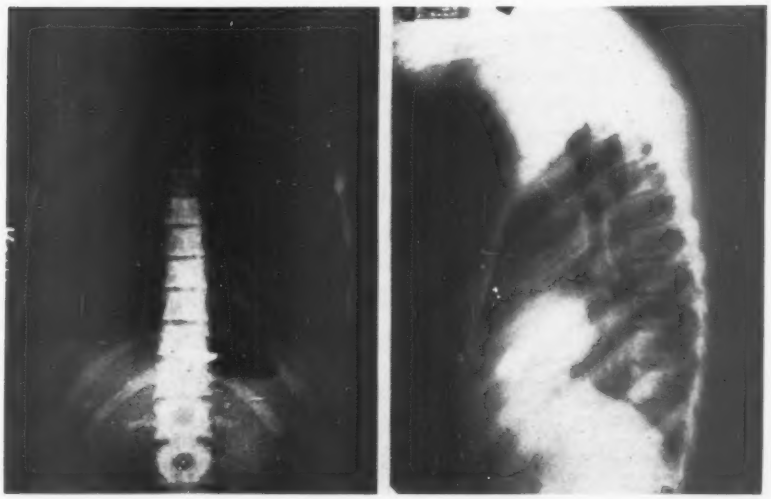


Fig. 20.—Posteroanterior and lateral roentgenograms showing a foreign body in a pericardial abscess.

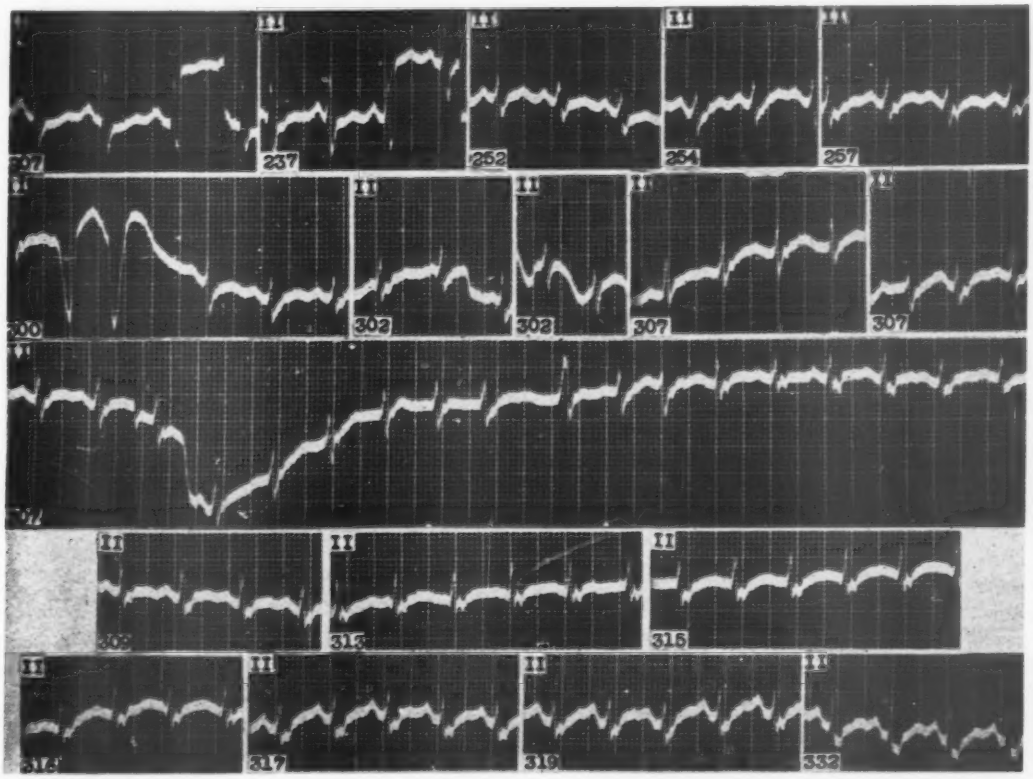


Fig. 21.—Electrocardiograms taken during the operation for removal of the pericardial foreign body. The number in the lower corner of each segment indicates the time (o'clock) the tracing was taken.

interval lengthened to 0.13 second, in contrast with the normal complexes which were present at 207 and 237 before cardiac manipulation. It is unfortunate that this abnormality was recorded in Lead II only, but it may be regarded as indicating, at least, intraventricular block or bundle branch block, probably of the *right* side. The abnormal QRS complexes persisted throughout the operation, but the complexes had returned to normal four days later. This delay in conduction was found, by direct visual inspection, to be correlated with dilatation of the right ventricle, certainly an unusual observation in the human subject. It may be considered, in part at least, a result of the increased time necessary for the conduction of the impulse through the greatly dilated right ventricle.

The intolerance of the heart to dislocation was demonstrated in this case in two ways: first, by the ventricular dilatation, with incomplete bundle branch block, and second, by varying types of arrhythmia and circulatory collapse. Dislocation of the heart may produce torsion of the great vessels and obstruction to outflow of blood, with fall in blood pressure resulting from the diminished cardiac output, and with ventricular dilatation from the increased resistance to blood flow.

This type of experience has led us to avoid the apical suture as a means of exposing inaccessible areas of the heart. Generally speaking, in elective cardiac surgery, the approach can be so planned that precise and comfortable exposure is provided for any part of the heart. The various techniques for approaching different cardiac areas and chambers have received consideration and illustration elsewhere.[5]

Experience has also demonstrated that the classical hemostatic cardiac grips, which are intended to provide a bloodless field, are badly tolerated. These maneuvers upset cardiovascular dynamics and should therefore be used only as means of last resort.

The intolerance of the heart to obstructed blood flow is in sharp contrast to its stability during other cardiac and intracardiac procedures. The surface of the heart was manipulated, sutures were taken in the muscle, and actual incisions were made into the chambers of the heart with little disturbance. It was felt that keeping the surface of the heart moist with warm saline or novocaine solution was important in reducing the degree of irritability. There were minor evidences of irritability, such as extrasystoles, wandering pacemaker (varying P-R interval), and even A-V nodal rhythm. Ususally these phenomena were not accompanied by any significant clinical manifestations. Such minor abnormalities were often produced by noncardiac procedures during anesthesia and operation. They were often evoked by endotracheal intubation, spreading of the ribs, and manipulations of the hilar and mediastinal structures.

More extensive manipulations inside the cardiac chambers by the exploring finger or forceps to remove intracardiac thrombus or foreign body were less well tolerated, though frequently no abnormalities were noted. Marked cardiac irregularity in the form of multiple ventricular extrasystoles was commonly seen. The patient with the three cardiotomies, already discussed, demonstrated

this particularly well. Fig. 11 shows the electrocardiogram obtained as the foreign body was grasped and extracted from the right ventricle. There were showers of ventricular extrasystoles from varying foci in both ventricles, producing runs of ventricular tachycardia up to sixteen seconds in duration. Direct observation of the irregular heart action and examination of the electrocardiogram did raise the fear of impending ventricular fibrillation. At the end of the procedure, however, upon the removal of the irritating forceps and missile from the ventricular chamber, the ventricular tachycardia ceased promptly and the P-R interval returned to normal in three beats. In our experience so far, these irregularities have been relatively benign.

SUMMARY

Evidence is presented in support of the following indications for the removal of some intracardiac foreign bodies: (1) to prevent embolus of the foreign body or associated thrombus, (2) to reduce the danger of bacterial endocarditis, (3) to prevent recurrent pericardial effusions, and (4) to diminish the incidence of myocardial damage. The additional factors of pain and cardiac neurosis are also considered.

The behavior of the heart during various types of manipulation is described. Dislocation of the heart from the position of optimal function is poorly tolerated, as are other procedures which upset cardiovascular dynamics by obstruction to blood flow.

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EXPERIENCES WITH DICUMAROL (3,3'METHYLENE-BIS-[4-HYDROXYCOUMARIN]) IN THE TREATMENT OF CORONARY THROMBOSIS WITH MYOCARDIAL INFARCTION

PRELIMINARY REPORT

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FOLLOWING the discovery, isolation, and synthesis of dicumarol the anticoagulant properties of this and allied substances were demonstrated in animals by Link and his co-workers[1] and by Bingham, Meyer, and Pohle.[2] Immediately, several groups of clinical investigators initiated studies to determine the effectiveness of this substance in the prevention and treatment of thrombophlebitis with and without pulmonary or other embolic phenomena.[3-6] The technique for its use and the remarkable success achieved are now a matter of established record.

Early in our studies at the Vascular Clinic of the New York Post-Graduate Medical School of Columbia University, we considered the possibility of the use of this therapeutic agent in the treatment of coronary thrombosis. It is extremely difficult to evaluate its effectiveness in a particular patient who has suffered from an uncomplicated attack of coronary thrombosis in its early stages since we are, at present, unable to predict with certainty which patient will have a rapid series of secondary episodes of thrombosis, which one will have one or more embolic phenomena, and which patient will prove to have an uneventful recovery from the immediate attack. It is recognized that the patient who has a series of episodes of thrombosis in different radicals of the coronary tree within a short period of time or whose original thrombus propagates, extending centrally and thus blocking off additional branches of the same coronary artery, has an increasingly serious prognosis with each episode or extension. Experience has clearly demonstrated that once a person has more than two episodes of thrombosis within a period of three to four weeks there is a strong likelihood that further episodes will follow and that the prognosis is poor. The author has personally cared for many patients through such a course, helpless to prevent repeated attacks of thrombosis and death. In the same manner, once a patient has developed a mural thrombus and has had one or more embolic phenomena, the prognosis is grave indeed; especially if the mural thrombus is in the right heart thus producing pulmonary emboli.

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The first patients in this group to receive dicumarol were selected because:

1. They had suffered repeated episodes of multiple thrombi in different areas of the coronary tree or the original thrombus had propagated. The clinical evidence for these criteria consisted of repeated attacks characteristic of the coronary syndrome with precordial pain, fever, leucocytosis, and increased sedimentation rate, with confirmatory electrocardiographic findings.

2. They had suffered repeated embolic phenomena either pulmonary or to other areas. (It was recognized that certain of the pulmonary emboli might have arisen in the extra cardiac circulation, but following myocardial infarctions the percentage of pulmonary emboli is a considerable one and, from whatever source, repeated pulmonary emboli have an increasingly serious prognosis.)

3. They had evidence suggesting that both Factor 1 and Factor 2 were active.

Unfortunately, previously compiled adequate statistical data regarding the prognosis of each of these special categories in patients not treated by anticoagulants are unavailable. This fact combined with the difficulty of running a properly controlled series for each of the suitable subdivisions has mitigated against the drawing of final conclusions regarding the value of dicumarol in the treatment of coronary thrombosis.

The first patient in this series was treated with dicumarol in May, 1942. Since then, 76 patients with acute or recurrent coronary thrombosis have been treated with dicumarol by the author or under his direction.[7] These have been in both civilian and Army hospitals. Forty-three of these were selected because they qualified under one of the aforementioned categories as having a serious prognosis. Twenty-eight had evidence of multiple thrombi or propagation, 12 had multiple embolic phenomena, and three showed evidence of both types of episodes.

The experience with these groups encouraged us to increase the series by using this substance in 33 patients suffering from uncomplicated first or second attacks of coronary thrombosis.

In addition to dicumarol, all patients received conventional treatment including rest, opiates, barbiturates, aminophylline, and oxygen according to the indications.

A total of 15 patients died: 11 from the series of 43 with the more serious prognosis and four from the series of uncomplicated cases. Only four of the deaths occurred as a direct immediate result of the insult of the thrombosis. Three of these were in the complicated group and only one was in the uncomplicated group. Eleven deaths occurred as a result of cardiac failure two or more weeks after their last acute episode. Of these, eight were in the complicated group and three were in the uncomplicated group. Eight autopsies were performed. No evidence of hemorrhage or any other effects of dicumarol, which could have produced death, were found. The livers from three patients showed slight fatty infiltration which was not considered to be of serious degree. Of the

43 patients in the complicated group, 38 ceased having evidence of extension, additional thrombi, or embolic phenomena after the dicumarol therapy was inaugurated.

Sixty-one patients recovered from the attack during which this study was carried out. While the over-all mortality figures do not differ markedly from the anticipated rate for single attacks of coronary thrombosis, certain facts should be considered in this regard.

1. Forty-three of these patients were selected because they had complications known to be associated with a very high mortality. (As mentioned previously, exact figures are not available but 60 to 70 per cent mortality would approximate the anticipated risk of this group of patients in the experience of the author.) Only 11 (25 per cent) of these patients died in the episode for which they were treated.

2. Of the 33 patients having their first or second uncomplicated attack at the time of onset of treatment with dicumarol, four died (12 per cent) against an anticipated death rate of 20 to 30 per cent.

The observation of individual cases seemed more suggestive. Abstracts of several case histories of particular interest are therefore included.

CASE HISTORIES

CASE 39.—A 50-year-old man was admitted to the hospital complaining of severe precordial pain of four hours' duration which radiated down the left arm. He had suffered from one previous recognized attack of coronary thrombosis nine months before. The first attack had been diagnosed on the basis of precordial pain with prostration, fever, increased sedimentation rate, leucocytosis, and electrocardiographic tracings typical of an anterior myocardial infarction. The patient was hospitalized for ten weeks and made an uneventful recovery; he had only the single moderately severe episode. He was able to return to administrative work and, aside from easy fatigability, had no marked untoward effects.

The second attack, during which the patient was hospitalized, was accompanied by more severe pain and breathlessness. The second day the oral temperature reached 101° F. The sedimentation rate rose until on the seventh day it reached 62 mm. per hour. The white count increased to 12,400 with 78 per cent polymorphonuclear cells. The electrocardiogram which was normal on admission showed changes on the third day typical of an acute anterior infarction as follows: there was a convex S-T segment with late inversion of the T waves in Lead I, a concave S-T segment in Lead III, and an absent Q wave with an upright T wave in Lead IV. Serial tracings showed changes which tended to revert toward normal by the tenth day. On treatment with rest, morphine, and whiskey he did well. By the twelfth day the patient was comfortable, the fever had subsided, and the sedimentation rate was down to 28 mm. per hour. He appeared to be on the way toward an uneventful recovery when suddenly he was seized with an agonizing precordial pain and once more developed fever which reached 103° F. This time the course was much more stormy. He required oxygen therapy for his dyspnea and cyanosis, his liver edge extended down 2 fingerbreadths below the costal margin and was tender, and the sedimentation rate increased to 70 mm. per hour. The white cell count rose to 16,000 with 80 per cent polymorphonuclear cells. The electrocardiogram showed marked changes again, but this time they were typical of a posterior myocardial infarction with some residual changes from the anterior infarction as follows: T_1 was isoelectric and there was a concave S-T interval with a high origin in Lead II, a deep T_3, and absence of R_4 with deep T_4. The rhythm was regular.

A third episode occurred seven days later and his precordial distress became more constant. He was dyspneic and cyanotic and was kept in an oxygen tent constantly. The electrocardiogram showed further disturbance suggestive of posterior wall damage.

Dicumarol was started immediately after the third attack in the hope of decreasing the tendency toward further thromboses. It was administered according to the technique outlined later in this paper. The prothrombin time was kept as closely as possible between 30 and 35 seconds for thirty days. The patient's course was uncertain for one month but he gradually improved and after three and one-half months he was having only moderate discomfort and was able to leave the hospital. There were no evidences of the formation of additional thromboses nor of propagation of former thromboses after the inauguration of dicumarol therapy.

As noted earlier in this report no one can say with certainty whether or not dicumarol influenced the course of this patient by tipping the balance away from a tendency toward thrombosis. Nevertheless, this type of history was repeated sufficiently often in this series to warrant giving serious consideration to the possibility of such an action.

CASE 42.—A 36-year-old man was admitted to a hospital complaining of precordial pain of moderate severity and without radiation. He had suffered from the anginal syndrome produced by effort for two months prior to the present acute episode. He had an oral temperature of 100° F. on admission. The second day this rose to 101.5° F. and then slowly subsided. On rest with morphine, the pain disappeared within thirty hours. The sedimentation rate reached a peak of 36 mm. per hour on the fifth day and the white count reached 11,400 with 76 per cent polymorphonuclear cells. The electrocardiogram showed typical changes of a posterior (T_3 type) myocardial infarction on the second day with a tendency toward reversion to normal by the seventh day. His course was mild. By the sixth day he felt so well that it was difficult to keep him in bed. On the ninth day he had a sudden sharp pain in the right posterior chest associated with some difficulty in breathing comfortably. The next day he coughed up bright red stained sputum. A pleural friction rub was readily heard over the right lung base posteriorly on normal breathing. No evidence of peripheral thrombophlebitis could be found on physical examination. X-ray films showed a shadow characteristic of a small pulmonary infarction in the right lower lobe laterally.

Four days later there was a recurrence of acute pain in the right lung base posteriorly and again bright red blood was raised by coughing. Two days after the second episode a third one occurred, this time in the left lung base.

It was believed that the patient had developed a mural thrombus in the right heart, following his myocardial infarction, from which segments of fresh thrombus were breaking off to become pulmonary emboli. The possibility of an undetectable thrombus existing in an extra cardiac vein was also considered as a source of the pulmonary emboli.

Regardless of which source was correct, anticoagulant therapy appeared logical and dicumarol was given according to the technique set forth elsewhere in this paper. It was continued for one month.

During the first two weeks a prothrombin time of approximately 30 to 35 seconds was maintained. During the second two weeks this was gradually allowed to revert toward normal. No further pulmonary emboli occurred after the dicumarol therapy was started.

While it is recognized that minute pulmonary emboli may occur which cannot be diagnosed during life, we can safely state that none of clinical significance occurred following the use of dicumarol. Again we cannot prove beyond a doubt that dicumarol affected the course of this syndrome, but the possibility is certainly worthy of consideration.

CASE 18.—A 47-year-old man was admitted to the hospital Nov. 26, 1942, complaining of increasing dyspnea on exertoin. He gave a history of hypertension which was first recog-

nized in 1934. Between 1934 and 1942 the systolic blood pressure had varied between 160 and 200 mm. of mercury. He did not know the diastolic pressures. The patient had no symptoms. One brother and two sisters had hypertension. In August, 1942, the patient observed that he became dyspneic after walking only three blocks. This was fairly constant. One evening (exact date uncertain) in September, 1942, about 8:00 P.M., while lying in bed, he suddenly became very dyspneic. He began to wheeze and at the same time developed pain in the lower substernal area which radiated to the shoulder. This attack lasted fifteen minutes and then completely disappeared without medication. A blood pressure reading taken shortly afterward showed the usual elevation. There was no history of previous attacks of breathlessness or of any form of allergy.

On physical examination on admission, the patient did not appear ill. The blood pressure averaged 200/150. He had an emphysematous type chest that was hyperesonant to percussion. There were no râles in the chest. The fundi showed copper-wire arteries. All peripheral pulses were strong. The heart was enlarged to the left and downward. The apex beat was felt just lateral to the mid-clavicular line in the sixth intercostal space. At times a triple thrust was felt in the apex region. There was a booming first sound at the apex and an accentuated aortic second sound. No murmurs could be heard. There was occasionally a gallop rhythm at the apex accompanied by pulsus alternans. No friction rub was heard.

Blood counts, serology, and urine analysis were normal. The highest sedimentation rate was 30 mm. per hour. X-ray films of the chest indicated left ventricular enlargement and some pulmonary congestion. The first electrocardiogram revealed left ventricular preponderance and evidence of myocardial damage compatible with a previous anterior myocardial infarction (T_1 type).

The day after admission the patient became dyspneic. The liver was enlarged to about 4 cm. below the costal margin. The neck veins became engorged and moist râles were heard in the chest. Mercupurin was given; diuresis ensued, the râles disappeared, and the liver became smaller. It was necessary to give mercupurin about every five days in order to keep the urine output approximately equal to the intake. On the fourteenth day after admission the patient developed epigastric pain, wheezing, and went into mild collapse. The pulse became rapid and thready and the blood pressure dropped to 140/90. A low-grade fever was noted. Electrocardiographic studies showed evidence of a superimposed anterior infarct (T_1 type with coving). A pericardial rub developed at the apex. At this time a left ventricular aneurysm was suspected on the basis of x-ray findings. Because of the prognosis and the possibility of propagation of the original thrombus, the development of new thrombi, and the development or extension of mural thrombi we decided to use dicumarol. It was administered according to a somewhat lower schedule of dosage than outlined elsewhere in this paper, the prothrombin time being kept between 26 and 30 seconds. A total of 1,500 mg. of dicumarol was given. No evidences of hemorrhage were ever noted.

On the twenty-first day the patient went into mild peripheral failure and pulmonary edema. Digitalis was then cautiously administered. On the thirty-first day ventricular extrasystoles developed. Quinidine was given to prevent ventricular fibrillation. On the thirty-second hospital day the patient slumped forward in bed and died suddenly.

The significant autopsy findings were as follows: The pleural, pericardial, and peritoneal cavities were free from excessive fluid. The lungs were slightly heavy and more reddish brown than usual. No infarctions were noted. On section the alveolar walls were thickened in some areas and ruptured in others. The heart weighed 570 grams. It presented the configuration of the essential hypertensive heart with hypertrophy of the left ventricle. At the apex there was a small aneurysm of the left ventricle which measured 3.5 cm. in diameter. It projected out about 1.5 cm. beyond the surrounding heart tissue. The left coronary artery was tortuous and contained numerous calcific plaques. Just beyond the origin of the left coronary artery the lumen was obliterated by dense, grayish-white tissue apparently representing an old organized thrombus. The area of occlusion measured 1.8 cm. in length. Five centimeters beyond the distal extremity of this thrombus another occlusion was

present. It measured 0.5 cm. in length and consisted of reddish-gray, somewhat stratified, tissue. The right coronary artery showed only slight atherosclerosis. Section through the heart revealed the middle part of the major portion of the left ventricular myocardium to consist of yellowish, necrotic, fattylike tissue. The area of necrosis measured 4 to 7 mm. in width. The subepicardial and subendocardial myocardium adjacent to the infarct appeared grossly normal. The wall of the aneurysm measures 3 mm. in thickness. Two of the intertrabecular recesses of the aneurysmal portion of the left ventricle contained dry, granular, reddish-gray masses representing a small mural thrombus. The outer surface of this mural thrombus appeared to be well sealed off by fibrin. The myocardium of the interventricular septum showed extensive areas of scarring. The left ventricular myocardium measured 14 mm. in thickness. The right ventricular myocardium measured 3.5 millimeters. The valves were competent and of tissue paper thickness, and the circumferential measurements were within normal limits. Histologic sections showed all gradations between frank necrosis and early degenerative changes in the left ventricular myocardium. A section of the mural thrombus indicated that it was relatively recent consisting of irregular anastomosing homogeneous acidophilic laminae with the spaces between containing fibrin, red blood cells, and leucocytes. Five sections of the left coronary artery were studied. In all five sections, the intima was markedly thickened by a connective tissue matrix containing calcific deposits, clefts having the configuration of cholesterol ester crystals, and scattered lymphocytes. In several other sections the lumen was either completely obliterated or reduced to small slitlike apertures. In one section the lumen was occupied by an organized thrombus and was partially recanalized. In other sections the vessel contained a relatively recent ante-mortem thrombus.

The determination of the effect of dicumarol in this case is difficult, if indeed any can be demonstrated. The dosage was small and the prothrombin time was kept lower than was the case with later patients. This case does illustrate clearly the complicated picture which is not infrequently encountered. We found evidence of one large and multiple small occlusions, at least some of which may well have occurred at the time of the acute episode of September, 1942. A major recent occlusion was found in the more distal portion of the left coronary artery. This probably occurred with the acute episode of Nov. 12 to 13, 1942. There was evidence of acute myocardial infarction, a ventricular aneurysm, and, of particular interest in this instance, a small mural thrombus in the aneurysm. If this thrombus increased in size, it was perfectly capable of liberating emboli. It was, however, sealed over and no embolic phenomena were discovered. Whether dicumarol played a part in preventing emboli in this case we cannot say. Its use would seem indicated. As in Case 21 dicumarol could have no effect on the course of the condition once the myocardium was sufficiently severely damaged.

CASE 21.—A 42-year-old man was admitted to the hospital complaining of "tearing" substernal pain which radiated into the neck. He developed a fever of 103° F. on the second day. His sedimentation rate rose to 46 mm. per hour and the highest white count (fourth day) was 12,400 with 77 per cent polymorphonuclear cells. The electrocardiogram showed the pattern of anterior myocardial infarction (T_1 type). On routine treatment he improved for six days. Suddenly, while eating, he was seized with a severe pain in the right lateral chest which persisted for two days. The second day he coughed up bright red blood. No friction rub could be heard, but an x-ray film showed a shadow compatible with a pulmonary infarction in the right lower lung field. His heart then developed auricular fibrillation and began to show evidence of decompensation. The following day he had a second similar pulmonary episode in the left base and two days later one in the right middle lung field.

Dicumarol was started on the ninth day and administered according to the technique outlined in this paper. No further recognizable embolic phenomena occurred after dicumarol therapy was instituted. The patient, however, pursued a progressively downhill course and became more severely decompensated. He became orthopneic, moist râles were heard first over both lower lobes, later throughout both lungs. His liver became enlarged and tender, and dependent edema appeared. Oxygen therapy, aminophylline, mercurial diuretics, and digitalis were used without favorably affecting the course of the patient.

He expired thirty days after the onset of his attack and twenty-one days after dicumarol therapy was instituted. The prothrombin time had fluctuated rather widely during the disturbance in fluid equilibrium occasioned by the decompensation, ranging from 23 to 52 seconds, but at no time was there evidence of any hemorrhagic manifestations other than a small purpuric spot on the left thigh and some minor hemorrhagic areas at the sites of venipuncture in both arms. These were such as might be seen in the absence of dicumarol therapy.

Autopsy revealed the following significant findings: The lungs showed typical signs of congestive heart failure. In addition there were evidences of one large, old infarct in each lower lobe and of numerous scattered small infarcts. It was believed after examination that probably none had occurred within a period of two weeks before death. The liver weighed 1,345 grams and showed some evidence of passive congestion with cloudy swelling. The heart weighed 530 grams. Both coronary arteries were tortuous and contained numerous calcific plaques. Five centimeters from the origin of the right coronary artery the lumen was obliterated by a thrombus which was reddish-gray and stratified. It extended about 2 cm. and blocked off several branches of the artery. Sections from this area showed the myocardium of the right ventricle to consist of necrotic, yellowish, fattylike tissue. Microscopic studies showed typical findings of a recent massive myocardial infarction. Attached to the endocardial lining of the right ventricle was an olive-shaped, shiny, mural thrombus 1.5 by 3 cm. in size. On section it appeared to be relatively recent in origin but was completely sealed off by a layer of material resembling fibrin. Other evidence of possible sources of the pulmonary emboli, either intra- or extracardiac, could not be found. Several old occlusions of minute branches of the left coronary artery were found.

While we cannot say with certainty that dicumarol prevented the further propagation of the mural thrombus with a resulting cessation of pulmonary emboli, the following points are in favor of this possibility:

1. The episodes of pulmonary embolism ceased following the inauguration of dicumarol therapy. This was confirmed clinically and pathologically.

2. The mural thrombus, while recent in origin, was sealed off to a remarkable degree.

3. No other sources of pulmonary emboli were found. (The possibility of emboli coming from some obscure venous source was not completely ruled out.)

On the other hand, as anticipated, the use of dicumarol did not affect the course of the process once a massive infarct had occurred. The patient progressed into a condition of cardiac insufficiency and death.

DISCUSSION

It has been observed by numerous workers, and confirmed by the author, that when a thrombosis occurs either in a vein or an artery in one portion of the body it is common, either simultaneously or within a short time, for multiple thrombi to form in other parts of the vascular tree as well as for local propagation of the primary thrombus to take place. The exact mechanism which causes

this phenomenon has never been adequately explained. Perhaps the explanation is the simple one of decrease in the rate of blood flow which occurs secondary to placing the patient at complete bed rest, the most common procedure. Evidence against this hypothesis is found in the work of Baumgarten,[8] Dietrich,[9] and others who have demonstrated that blood does not coagulate in a vein that has been ligated carefully at both ends. We have found the clotting time and prothrombin levels to be within normal limits in patients whom we have checked during such episodes.*

The question of the relation of the platelets to this occurrence is worthy of comment. Hueck[10] and von Seemen[11] have reported a decrease in platelets during the first three to five postoperative days followed by a marked increase in number. Similar observations have been made in the presence of inflammation[11, 12] and malignant growths.[10, 13, 14] The agglutination tendency of the platelets is considered to be increased when the globulin fraction and the fibrinogen increase and the albumin fraction diminishes; in other words, when a shift occurs toward coarse dispersion in the relation between the protein components of the blood.[15] Such shifts tend to take place after operations and accidental trauma and in the presence of infections and malignant growths.

Starlinger and Sametnik[16] have reported that as the shift toward the more coarsely dispersed globulins occurs the normal electrical charge of the platelets, which is negative and hence repellent to the similarly negative proteins, diminishes. This decreases the tendency to repulsion and hence increases the tendency to agglutination.

Stuber and Lang[12] have proposed an explanation for the diminished electrical charge of the platelets. Their explanation is that a retarded circulation results in increasing the carbon dioxide in the blood. This increases glycolysis, which entails a decrease in the negative electrical charge of the thrombocytes with an accompanying increased tendency to agglutination of the thrombocytes.

The action of thrombokinase released from cells as a result of surgery, inflammation, or malignancy might weigh the balance in favor of coagulation and is worthy of further careful study. Numerous other factors have been discussed in this regard. For a review of this subject the reader is referred to the comprehensive monograph by Bruzelius.[17]

Multiple thrombosis is an extremely common occurrence in patients with thrombophlebitis; it probably occurs in the majority of patients. Here again available figures are of little significance since autopsy findings have revealed that many thrombi may be present in various venous segments without being detected, or indeed detectable, clinically.

That a similar phenomenon occurs in a definite group of patients with coronary thrombosis is clearly demonstrated by following the clinical and electrocardiographic findings. This occurs in the absence of surgery or other trauma, malignancy, and, in the strict sense, inflammation (at least without the basis of infection). These patients characteristically have a typical primary episode

*Recent unpublished work of Meyers and Poindexter suggests that minute increases in the prothrombin level of the blood may occur associated with coronary thrombosis.

followed at intervals of from seven to twenty-eight days or more by recurrent attacks of pain, fever, leucocytosis, and increased sedimentation rate, with electrocardiographic evidences of more marked involvement in the same area or multiple involvement in other areas of the heart.

Autopsy findings showing multiple undiagnosed occlusions of the coronary arteries also demonstrate that this phenomenon may occur without clinical recognition. Frequently a careful review of the history will reveal suggestive symptomatology which was not interpreted correctly by the patient or his doctor.

Do these multiple episodes of thrombosis occur because there exists a profound change in the thrombosing balance of the blood which is responsible for the first and the subsequent thrombi wherever the vascular walls are conducive to this process? Is the change primarily a local one which initiates a generalized change in the thrombosing balance of the blood? Or is it primarily a widespread vascular change which produces a condition conducive to thrombosis in numerous focal points at approximately the same time? We cannot answer these questions for either thrombophlebitis or coronary thrombosis at this time.

It is logical, from a physiologic viewpoint and on the basis of clinical experience in the treatment and prevention of venous thrombosis and pulmonary embolism, to utilize anticoagulant therapy for the treatment of coronary thrombosis where there is evidence of a tendency to additional thrombosis either local, scattered in the coronary tree, or mural. It should be pointed out that with the development of mural thrombi, thrombosis of the thebesian veins may occur as a result of obstruction of their ostia. Cases have been observed where the thrombi in the thebesian veins propagated into the larger venous sinuses. This sequence of events tends to further damage the myocardium by interference with its nutrition.[18] This phenomenon is not as yet very widely recognized.

Dicumarol is the present drug of choice for this anticoagulant therapy. If the situation is very acute, heparin may be used for the first twenty-four to forty-eight hours until the action of dicumarol is established.

METHOD OF ADMINISTERING DICUMAROL

In our series the following techniques for administration have been used:

1. The prothrombin time is determined (Quick or Link-Shapiro undiluted technique*) before the first dose is given. The normal reading should be 13 to 17 seconds.

2. If the prothrombin time is normal or lower, 300 mg. of dicumarol are administered orally in one dose.

3. Each morning the prothrombin time is determined and reported to the physician in charge of the case *before* the dicumarol dosage for that day is determined.

4. Dicumarol is administered in 300 mg. doses daily until the prothrombin time is 30 seconds, and in 100 or 200 mg. doses when the prothrombin time is between 30 and 35 seconds on the upward portion of the curve.

*The thromboplastin used must be fresh and checked against a control for each test. The use of thromboplastin giving high control figures may prove dangerous in misguiding the dicumarol dosage.

5. When the prothrombin time reaches 35 seconds dicumarol is discontinued until it drops to below 30 seconds, when the drug may be given cautiously in 100 to 200 mg. doses again.

6. Daily prothrombin times are determined. Frequently the time may rise for several days after discontinuing dicumarol but will then return toward normal. If it reaches 60 or more seconds, hemorrhagic manifestations may occur. In this series, these were confined to minor purpuric spots in three patients.

7. If more severe hemorrhagic manifestations should occur, they may be checked by one or two whole *fresh* blood (may be citrated) transfusions of 300 to 500 c.c. each, by the administration of vitamin K (Menadione bisulfite, 64 mg., in from one to four doses has proved satisfactory), or both.

8. Dicumarol has been continued in most of these patients for thirty days after the last episode of thrombosis or embolism. The objective has been to keep the prothrombin time between 30 and 50 seconds especially during the first two to three weeks. The dosage is then tapered off slowly permitting the time to drop to 25 to 30 seconds followed by a gradual return to normal.

SUMMARY AND CONCLUSIONS

It would be premature to make extensive claims about the merits of dicumarol in the treatment of coronary thrombosis. Adequate controls with which to determine its value statistically are not yet available and will be of little value unless several subdivisions depending on the severity, extension, and complications of each group are studied separately. Each of these subdivisions must contain a statistically significant number of controls and treated patients. This will be a long and difficult but important evaluation.* It did not seem justified to await the final results of such a study before reporting on the experiences contained in this paper. We can conclude the following from these experiences.

1. In no case was there evidence that dicumarol aggravated or complicated the course of a patient with coronary thrombosis. The possibility that intimal hemorrhage[19, 20] might be a complicating factor was considered, but no evidence was obtained in this series, either clinically or pathologically, that this was of significance in any case.

2. On the basis of previous animal and human experience with dicumarol, it appears physiologically sound to use it whenever there is a definite tendency for a thrombus to propagate or multiple thrombi or embolic phenomena to occur. Certain cases of coronary thrombosis demonstrate definite tendencies in this direction.

3. In numerous individual cases it has appeared that these thrombosing and embolic tendencies have been interrupted by the use of dicumarol. Considering the degree of pathologic narrowing of the coronary arteries found in some hearts, it is not surprising that occlusions did continue to occur in some patients on dicumarol therapy.

*Such a study is being planned as a cooperative venture in ten hospitals under the auspices of the American Heart Association.

4. The mortality rates for the complicated and the uncomplicated cases of coronary thrombosis treated with dicumarol appear to be lower than anticipated for each group, but it is considered inadvisable to draw conclusions regarding its effect on the mortality rate on the basis of so small a series and without careful controls. Another factor which may have influenced these figures favorably is the fact that the average age was younger than that usually considered average for patients with coronary thrombosis. Fifteen were under 35 years of age; only ten were above 60. Much more study is esential to determine this point.

5. In no instance was it felt that dicumarol influenced the rhythm or the rate of the heart directly.

This study suggests that dicumarol may be of value as a preventive measure against propagation, multiple serial attacks of coronary thrombosis within short spaces of time, mural and thebesian vein thrombosis, and embolic phenomena following coronary thrombosis. A study of the use of dicumarol in the treatment of such complications when associated with auricular fibrillation also seems justified. The value of the routine use of dicumarol in all cases of coronary thrombosis has been considered. The material available to date does not, however, justify the conclusion that dicumaroi will affect the results in uncomplicated cases of coronary thrombosis.* It is also impossible to state to what degree it will affect the longevity of a patient with marked progressive arteriosclerosis of his coronary arteries. Further investigation with large groups of such patients will be necessary to determine the answer to these questions.

There is no evidence that once dicumarol has been discontinued and the blood prothrombin level has returned to normal any effect is exerted which decreases the risk of further attacks of coronary thrombosis in the same individual. Its continued use as a preventive measure may be a subject for future studies, but the risk of the use of this substance without careful frequent observation of the prothrombin level in the blood must be borne in mind.

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THE NEUROVASCULAR SYNDROME AS MANIFESTED IN THE UPPER EXTREMITIES

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OVER a period of many years much has been written on vascular and neurological syndromes which result from anatomic anomalies in the neck and shoulder girdle. It is not the purpose of the author to review the literature dealing with these anomalies, nor to outline the differential diagnostic features. Wright[8] has recently well provided this information in his article describing the neurovascular syndrome produced by hyperabduction of the arms (Figs. 1*A*, 1*B*, 1*C*, and 1*D*) in persons not necessarily having any anatomic anomalies in the neck or shoulder, such as extension of transverse processes and cervical ribs of the lower cervical vertebrae,[1-4] tendinous or cartilaginous extensions or counterparts of cervical ribs,[6] scalenus anticus,[5, 6] abnormal costoclavicular compression,[3, 7] ruptured cervical nucleus pulposus, extrinsic or intrinsic tumor of the cervical cord, ulnar or median nerve injury, etcetera.

This case report describes a patient with complaints which, but for Wright's recent article,[8] would very probably have been diagnosed as "scalenus anticus syndrome" only, while actually this represents an example of the "hyperabduction neurovascular syndrome" as well. This material is offered so that the latter syndrome may be more frequently in examiners' minds, more zealously sought for, more frequently recognized, and more properly treated. Certain observations and recommendations as to treatment may be worthy of consideration. Relief from long-standing symptoms rapidly followed after the treatment outlined was initiated in this case. The relief may, however, have been unrelated to or only partially due to the treatment.

CASE REPORT

A white man, 52 years of age, of temperate habits but for smoking two and a half packs of cigarettes daily, was unable to recall any illness, operations, or injuries which might have played a role in the precipitation of his present illness.

In January, 1943, while on Army transport duty he spontaneously and gradually developed a pain in the region of the distal anterior aspect of the right biceps muscle. This pain became extremely severe. It was unaccompanied by tenderness, paresthesia, hypesthesia, numbness, or tingling. Passive or active motion of the right humeroscapular and elbow joints and pronation or supination of the right forearm greatly aggravated the pain. Anodynes, heat, massage, and manipulation of the afore-mentioned joints failed to relieve this pain, but it gradually subsided, disappearing about April, 1943. In July, 1943, the pain spontaneously and gradually returned, this time bilaterally. It was not at this time aggravated by the motions which had proved aggravating from January to April, 1943. He now observed the pain to be aggravated bilaterally by allowing his shoulders to be depressed toward his hips while his arms were at his sides and to be more distressing at night than by day.

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The pain was now, as before, essentially constant with fluctuations in severity. It was partially relieved if, while sitting, the patient placed his elbows on a table or on the arms of a chair, and if, while lying prone, he allowed his forearms to hang over the sides of the bed toward the floor. His customary sleeping position had been the prone position with his arms hyperabducted above his head and approximately parallel to the longitudinal axis of the body (Fig. 1*A*). The symmetrical pains developing in July were from the onset accompanied by bilateral ulnar hypesthesia, bilateral median and ulnar numbness and tingling, essentially constant pain in the left forearm and hand, and recurring episodes during which

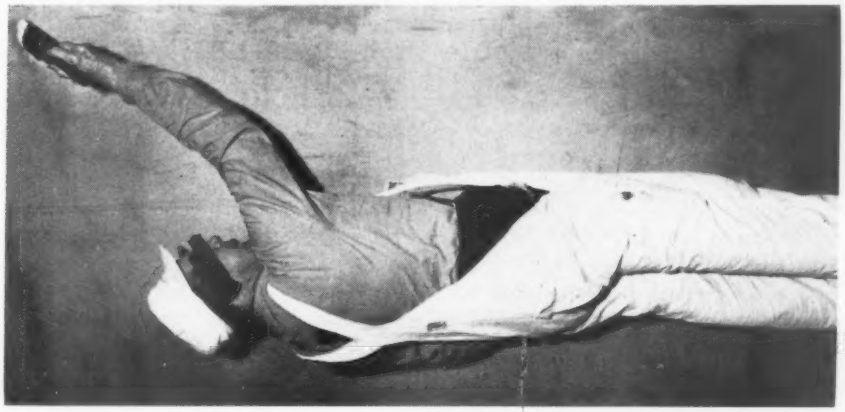

Fig. 1*C*.

Fig. 1*A*.

Fig. 1*B*.

Figs. 1*A*, 1*B*, and 1*C*.—For the purposes of this article these poses all portray what is described as hyperabduction of the arms. The word hyperabduction is herein used for lack of a more accurately descriptive term.

his left forearm felt cold. An extended course of generous doses of thiamine hydrochloride parenterally administered elsewhere had failed to give relief. The persistence of severity of the symptoms resulted in his hospitalization April 30, 1945.

The physical examination on this date revealed: (1) Hypesthesia over the areas innervated by the ulnar nerve, bilaterally; (2) obliteration of the right and reduction in amplitude of the left brachial pulse when the patient's arms were actively or passively hyperabducted (about 160 degrees) above his head when he was in the erect position (Fig. 1*C*); (3) obliteration of the right and reduction in amplitude of the left brachial pulse when the patient rotated his head to the left or right, respectively, with his arms abducted laterally 90 degrees from his body (less extreme rotation of the head was required to obliterate the pulses if the subject was obliged to rotate his head against the resistance of the examiner); (4) the development, in about three minutes, of bilateral ulnar numbness and tingling on the assumption of the positions portrayed in Figs. 1*A*, 1*B*, and 1*C* (this numbness and tingling developed even with a degree of hyperabduction insufficient to obliterate the radial pulses and regardless of whether the patient was erect, prone, or supine); (5) failure of the brachial pulse to return for two to five seconds after the obliterating positions had been abandoned, the interval increasing somewhat with extension of the time obliterating position had been maintained; (6) the shoulder girdles to be lightly muscled and normally or subnormally free in shoulder elevation and in hyperabduction of the arms.

Active or passive extreme depression of the shoulders with the arms at the sides failed to obliterate or reduce either brachial pulse; passive forcing of the shoulders posteriorward and downward failed to obliterate or reduce the amplitude of either brachial pulse.[3-7] Unfortunately, the author forgot to determine if prolonged depression of the shoulders toward the hips or downward and posteriorward would produce symptoms. It would seem likely, however, that symptoms would have resulted, for the patient stated in his history that his arms and hands pained and tingled when permitted to hang at his sides when he was in the erect position. This pain and tingling was very favorably influenced by removing the weight of the upper extremities from his shoulders by resting his elbows on a table or the arms of a chair. No reflex changes were demonstrable. Oscillometric and surface temperature studies were not available.

X-ray studies of the cervical and thoracic spines revealed only a slight scoliosis in the region of the fifth thoracic vertebra, with the concavity to left. X-ray studies of the sinuses revealed a marked uniform density througout the left antrum.

The blood count, blood Kahn, blood sedimentation rate, blood urea nitrogen, urinalysis, and x-ray studies of the heart and lungs were normal.

The symptoms and findings lead the examiner to the conclusion that the patient probably had both the scalenus anticus syndrome[5, 6] and the "neurovascular syndrome produced by hyperabduction of the arms,"[8] described by Wright. The amount of vascular element in the clinical features of this particular case is difficult to evaluate, for the brachial plexus, bilaterally, reacted to hyperabduction of a degree insufficient to obliterate the brachial pulses, and bilaterally reacted with the development of symptoms when the arms hung at the sides with the patient erect, though even an extreme of this latter position failed to obliterate either radial pulse. This case seemed not involved by the presence of a cervical rib. Whether or not a tendinous or cartilaginous band in the place of a rudimentary cervical rib was present[6] and acted in the manner of its counterpart was not determined; that it was the chief causative factor appeared unlikely. A ruptured cervical nucleus pulposus could possibly be present and causative; this, too, appeared unlikely in the absence of x-ray evidence of such a condition. Wright[8] reported that the obliteration of the radial pulse by hyperabduction of the arms is difficult and frequently impossible to produce in "loose jointed" individuals.

Since stretching or tension of the nerve trunks and brachial plexus is among the possible causes of the symptoms under study, it was decided to direct the patient to practice certain exercises and maneuvers which, it was believed, would possibly slowly lengthen the nerve and vascular structures, thus reducing the amount of tension to which they would be subjected and

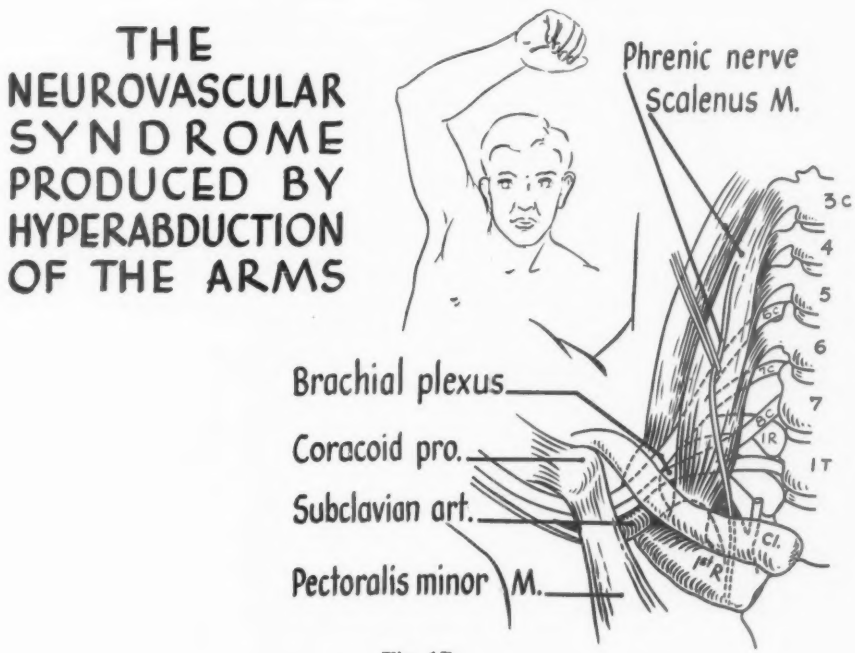

Fig. 1*D*.

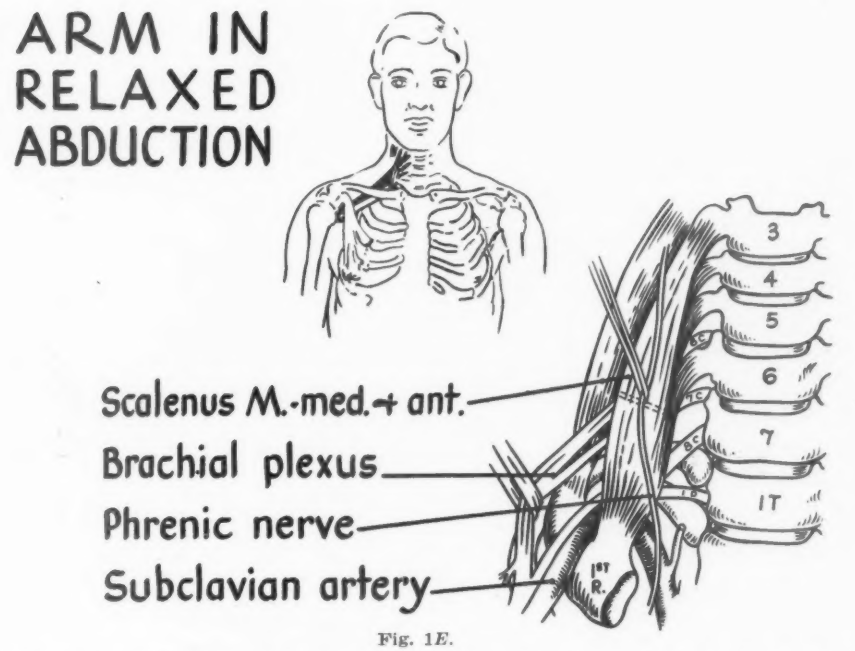

Fig. 1*E*.

Figs. 1*D* and 1*E*.—These figures are included for more graphic exhibition of anatomic relation ships in various positions.

would make the patient's shoulder girdles more "loose jointed." By stretching out the musculofascial structures which limit the excursion of the lateral angle of the scapula toward the midline of the body and cephalad, one reduces the acuity of the angle around which nerve and vascular structures are stretched as they pass under the coracoid process when the subjects's arms are hyperabducted. This same stretching would also tend to widen the costoclavicular space. The maneuver outlined to relieve the intolerance to the hyperabduction position consisted simply of the patient's suspending himself by closely approximated hands while he relaxed his shoulder girdle muscles (Fig. 2). He was to so suspend himself three or four time a day for such a period of time as comfort permitted. To build up the antagonists of the muscles we sought to stretch, the patient was directed, three or four times daily, while erect and with a 10- to 20-pound weight in each hand, to shrug or elevate his shoulders (Fig. 3).

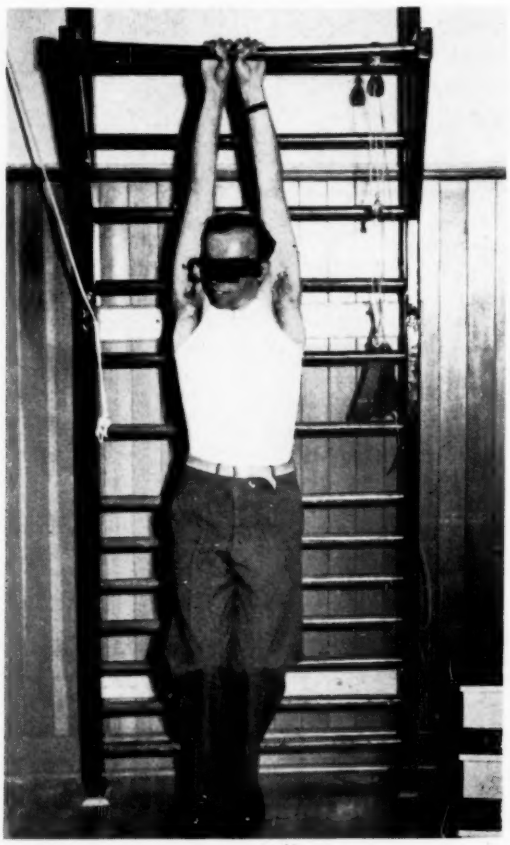

Fig. 2.

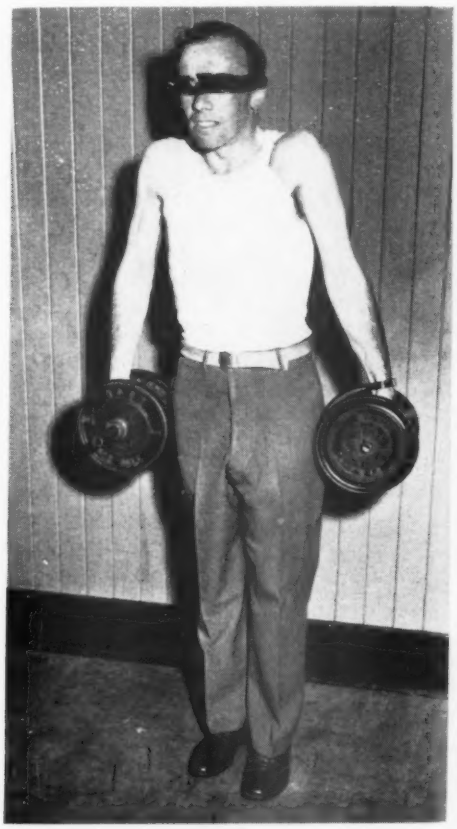

Fig. 3.

Fig. 2.—The position of suspension of the body by closely approximated hands, while shoulder girdle muscles are relaxed as completely as comfort permits.

Fig. 3.—The position of "shrugging" or elevating the shoulders against weighted resistance. The shoulders are actively elevated and passively relaxed or depressed alternately, thereby developing the elevators of the shoulders, better equipping them to hold the points of the shoulders higher without conscious effort.

If this patient's shoulders could be raised by developing the elevators of the shoulder, the acuity of the angle of the neurovascular structures as they pass through the angle formed by the first rib and the scalenus anticus muscle would be reduced. This should, it was believed, reduce the irritation to these structures at this musculoskeletal angle. Elevation

of the shoulder would also increase the costoclavicular space, lessening the hazard of pinching neurovascular structures at this point. These maneuvers and exercises were initiated about May 12 and were continued after the patient's discharge from the hospital, May 18, 1945. The patient was also directed to change his sleeping position to one in which his arms were not held in hyperabduction (Fig. 1*A*).

He reported improvement at the time of discharge, and on June 22, 1945, wrote, "My shoulders feel much better since taking the 'chinning' exercises. There is no pain in my left arm or hand. You will recall that when I was in the hospital, that was where I was bothered most. I still get the tingling sensation in the fingers in certain positions. My right wrist and right hand have bothered me and that appeared to be brought on by the chinning exercise. I appreciate the advice which I received about the shoulder exercises. I am continuing the exercises." About June 25 he reported by phone that the pain in his right wrist and hand had disappeared. On Sept. 1, 1945, the patient returned for re-examination. He then reported that the disturbing symptoms had disappeared and had not returned; that he had had no numbness or tingling in either arm or hand since about July 1; and that the pain earlier reported in the right wrist and hand still tended to recur infrequently, to last but a few days, and to develop and disappear gradually. The physical findings, September 1, were similar to those found April 30 on admission to the hospital except that the bilateral ulnar hypesthesia had disappeared and the shoulder girdles seemed more "loose jointed."

During his hospitalization in May, 1945, this patient exhibited keen interest as to the possible causative mechanisms and our aims in having him follow our suggested schedule of treatment. He has now quite completely abandoned his once customary sleeping position (prone with his arms in hyperabduction, Fig. 1*A*), and he now subconsciously rests his elbows on a table or chair arms when feasible. His new sleeping habits, his faithful exercise of the outlined treatment, or a combination of influences, some of which may not be clearly understood, may have produced the relief. This has occurred in spite of the persistence of certain physical findings which at the time of hospitalization seemed significant.

DISCUSSION

While the symptoms experienced by this patient probably resulted in part from obliteration of the arterial blood supply to the arms, it seems likely, in view of the prompt development of tingling in the fingers even when the arms were hyperabducted to a degree insufficient to obliterate the radial pulse, that changes in the nerve trunks resulted from prolonged stretching, pinching, or local ischemia, or some combination of these three factors. This does not, however, preclude the participation of arterial occlusion in the damage to the plexus and nerve trunks, for this patient's sleeping habits were such that he probably had pulseless brachial arteries for rather extended periods during his sleep. He habitually slept in the prone position and many, if not most, prone sleepers sleep with their arms in a position of hyperabduction and their faces turned toward one shoulder.

The obliteration of the brachial pulse by either the scalenus anticus syndrome or the hyperabduction syndrome may be due to either actual compression of the vessel so that its walls are opposed and lumen obliterated or to irritative spasm of the vessel. The fact that the radial pulse after obliteration does at times fail to return immediately on removal of the obliterating position or maneuver suggests that the latter is operative at times. This may explain Wright's observation[8] that certain positions of the arm, though unchanged, are accompanied by sudden changes in the presence or absence of a palpable radial pulsation.

This case demonstrates that, in the same person, several variations in the mechanisms responsible for irritation or damage of neurovascular structures of the neck and axilla may exist. This individual is believed to have both the scalenus anticus and the hyperabduction syndrome, each syndrome possessing identical or very similar symptoms but produced by different means. The former syndrome is produced by the irritation and/or obliteration of neurovascular structures at the angle formed by the attachment of the scalenus anticus muscle to the first rib, the latter syndrome by abnormal costoclavicular compression, or by torsion, tension, or compression of the neurovascular structures at the point where they pass under the coracoid process and posterior to the pectoralis minor muscle, or by both mechanisms together.

SUMMARY

1. Neurological and vascular syndromes, singly or combined, caused by various anatomic anomalies and changes in the neck and shoulder region, have long been recognized. Similar or identical syndromes, caused by a functional mechanism (hyperabduction of the arms) in the absence of anatomic anomalies have more recently been recognized and described by Wright.[8]

2. The recently reported, functionally produced syndromes[8] appear to be commonly produced (1) at the point where the vessels, plexus, and nerve trunks pass between the clavicle and first rib by costoclavicular pinching of the traversing structures, and (2) at the angle around which these structures pass under the coracoid process and posterior to the pectoralis minor, by torsion or stretching of the neurovascular structures. (Arterial spasm from irritation may in some cases contribute to the obliteration of the brachial pulse.)

3. Nonsurgical therapeutic suggestions, offered for consideration, are designed to: (a) avoid the positions responsible for the syndromes when practicable; (b) widen the costoclavicular space; (c) lengthen the involved neurovascular structures; (d) reduce the acuity of the angle these structures traverse as they pass under the coracoid process while the arms are hyperabducted; and (e) shorten the course traversed by these structures.

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POTENTIAL VARIATIONS OF THE RIGHT AURICULAR AND VENTRICULAR CAVITIES IN MAN

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IN THE five cases which form the basis of this report, an attempt was made to trace the course of the action current of the human heart directly by means of intracardiac catheterization. This seemed desirable because some of the fundamental concepts of electrocardiography have been evolved primarily from pertinent animal experiments, and assumptions concerning the course of the action current in the human heart have been made merely by analogy. Briefly, any electrical current of action can be considered as a line or layer of electrical dipoles or doublets so arranged that electropositive forces (source) are immediately followed by electronegative charges (sink).[1, 2] To electrical currents produced by the heartbeat, the laws which govern their flow in volume conductors have been applied.[2] It has been demonstrated that electrograms recorded from auricular muscle strips or from muscle in situ follow closely a predictable pattern based on formulas derived from such laws.[2-4]

The spread of impulses over and through cardiac muscle seems to be very similar in practically all species regardless of the presence of readily demonstrable conducting tissues.[5] Presumably no striking differences exist between the spread of the action current in the human heart and in the hearts of other mammals. The clinical use of precordial leads, for example, is based on the essential similarity in that respect of experimental electrocardiograms, particularly those of dogs, to those of man. For the study of the detailed sequence of activation of auricular and ventricular heart muscle, records from the endocardial as well as from the epicardial surfaces are required. Many such studies have been reported since the early observations of Lewis[6] and Lewis and Rothschild.[7] The admixture of cavity potentials to the precordial and standard limb lead electrocardiograms of the dog has led to newer interpretations of the pattern of bundle branch block, myocardial infarction, and myocardial infarction complicated by bundle branch block.[8-10] Again by analogy, the results of these observations on animals have been used in the interpretation of the abnormal human electrocardiogram.[11, 12] Epicardial leads have occasionally been recorded from human hearts but the potentials from the auricular and ventricular cavities needed to provide the final proof of the similarity of the human action current to that of experimental animals are lacking. It has been suggested that unipolar

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records from the right arm (V_R) and from certain esophageal leads reflect variations in cavity potentials. Leads of this kind are taken from positions located approximately opposite the large vascular openings at the base of the heart. This permits the potential variations of the ventricular cavities to be transmitted to the right shoulder and the right arm, or to the esophagus.[12, 15] The location of these leads with respect to cardiac muscle is such, however, that they cannot be expected to represent potential variations of purely intracardiac origin.

Cardiac and vascular catheterization through the antecubital veins, as practiced by Cournand and others, provides a relatively safe procedure for obtaining electrocardiograms from the right auricular and ventricular cavities and from the larger veins.[16] In the following experiments a No. 9 radiopaque catheter was used through which a small enamel-coated copper wire was threaded. The end of the wire was soldered to a small lead pellet which fitted and all but completely occluded the small opening at the tip of the catheter. This unit constituted the exploring electrode. A central terminal was used as the indifferent electrode. Under local infiltration with novocain, a right or left antecubital vein, usually the basilic vein, was exposed. Under fluoroscopic control the catheter was inserted and gently pushed ahead until the tip of the electrode was found to lie in the desired position. The patients were given sedation. Those in cardiac failure received 0.5 Gm. of aminophylline intravenously prior to the exposure of the cubital vein. All patients received 25 to 50 mg. of heparin to lessen the chance of intravascular clotting. None of the patients complained of pain or of discomfort of any kind, even when the tip of the electrode was seen to rest against cardiac muscle. No reactions or aftereffects were encountered. All patients received prophylactic treatment with sulfadiazine for two days after the procedure. X-rays and electrocardiograms were recorded frequently and at regular intervals.

The present report deals with the results obtained in five subjects. There were two instances of right bundle branch block (one complicated by a myocardial infarction two years previously), one of left bundle branch block, one of left ventricular enlargement, and one instance of left ventricular enlargement with frequent auricular and ventricular extrasystoles (bigeminus). On all patients standard bipolar limb leads, unipolar limb leads (extremity potentials), and serial unipolar precordial leads were obtained either immediately before or after the procedure. In one instance serial esophageal leads were recorded. Simultaneous records of either Lead I or of precordial Lead V_1 were made whenever feasible.

The records may conveniently be discussed according to the location of the tip of the electrode as determined by fluoroscopy.

Superior Vena Cava.—In two instances a record was obtained before the electrode had entered the heart itself. Both were patients with considerable left ventricular enlargement (one with associated signs of left auricular distention). The records revealed primary negative deflections for P and QRS, with positive T waves. The P waves were approximately one-half the size of QRS complexes and were double-notched in both instances, especially so in the case showing

evidence of auricular enlargement. The size of the deflections was of the order of those usually seen in unipolar extremity potentials, and their shape was almost identical with that observed in unipolar right arm leads (Fig. 1).

Inferior Vena Cava.—In one instance the electrode slipped into the inferior vena cava and down into a heaptic vein. The potentials recorded from the inferior vena cava were similar to those obtained from the superior vena cava,

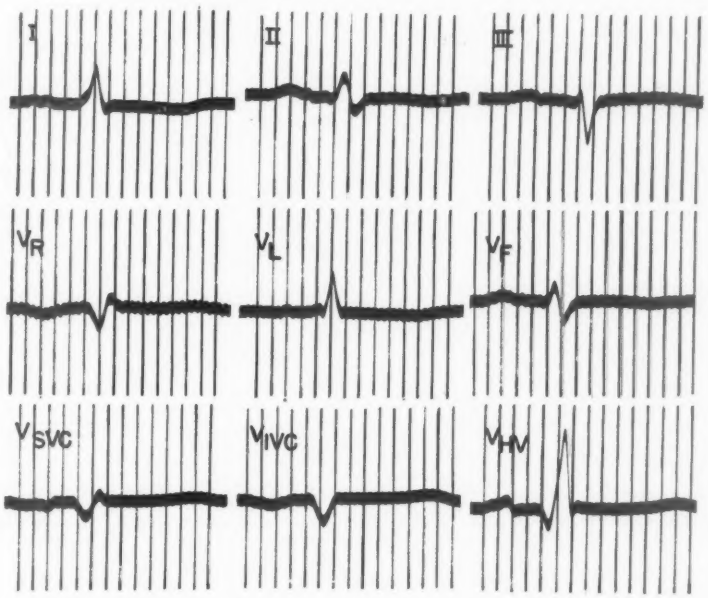

Fig. 1.—Leads I, II, and III, unipolar extremity potentials (V_R, V_L, V_F), and leads from superior vena cava (V_{SVC}), inferior vena cava (V_{IVC}) and from a hepatic vein (V_{HV}). Galvanometer sensitivity normal for standard lead and extremity potentials (augmented type), 0.75/N sensitivity for venae cavae and hepatic vein leads.

except that the auricular deflections were more rounded and the ventricular complexes lacked a small R wave which had been present before (Fig. 1). The record from the hepatic vein was quite different. A biphasic P wave was obtained, with a large slurred positive limb and a small negative spike. The ventricular deflections were primarily positive, displaying large R waves preceded by Q waves and followed by a small S deflection. The T waves were positive (Fig. 1). Neither the auricular deflections nor the ventricular complexes resembled those recorded in standard leads, extremity potentials (unipolar limb leads), or in any of six precordial leads. They were, however, of the left ventricular type, with a delayed peak of R (late onset of intrinsicoid deflection). The record appeared similar to those recorded by Helm, Helm, and Wolferth[15] from the duodenum.

Right Auricle.—With the exception of the case mentioned above, the electrode entered the right auricle proper in all instances and records were obtained from various auricular levels.

1. *Auricular Deflections:* The auricular deflections appeared similar in configuration to those obtained from esophageal leads at auricular levels and were

of the same magnitude or slightly larger. Endocardial auricular waves are always biphasic and display a distinct QRS type of deflection, and are often followed by a plainly visible auricular T wave.* In one instance the electrode was found to be located inside the right auricle, adjacent to the entrance of the superior vena cava. A large, completely negative deflection was recorded (P_{QS}), indicating that the electrode very likely was located at the region of primary negativity, the sinus node (Fig. 2, *A*). When the electrode was moved toward the junctional region, there appeared a small P_R wave which gradually increased,

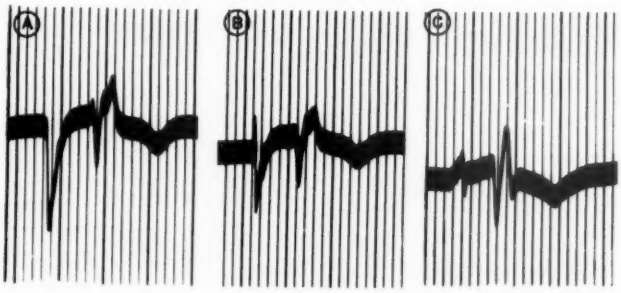

Fig. 2.—Case of right bundle branch block. (0.5/N sensitivity.) *A*, Large negative auricular deflection recorded from the immediate vicinity of the sinus node. *B*, Position of the exploring electrode slightly lower than in *A*; a small P_R wave has appeared, total voltage of P has decreased. Onset of intrinsic deflection for P occurs 0.005 second after beginning of P_{QRS}. *C*, Low auricular position (junctional region): small P wave with broad P_R deflection. Onset of intrinsic deflection for P: 0.060 second after beginning of P_{QRS}. Note change in contour of the ventricular deflection when the electrode is moved from upper to lower auricular levels.

so that at lower auricular levels a broad P_R, followed by a small sharp P_S deflection, was present (Fig. 2, *B* and *C*). A small P_R with a relatively large P_S was always noted in other records whenever the electrode was located in the upper auricular region (Figs. 3, *C*, 4, *E*, and 5, *A*). Occasionally the P_S deflection was broad: at times it completely occupied the space between the end of P and the beginning of QRS, which is usually isoelectric in standard limb leads (Fig. 3,*C*). Large P deflections with small or absent P_R are characteristic of upper auricular levels; large P_R waves with a decrease in the total voltage of P are typical of lower auricular or junctional levels. These findings are in agreement with those of Macleod and Cohn,[17] who obtained endocardial leads in cats with a comparable technique. In one instance a biphasic P wave with a predominant P_R deflection was obtained when the electrode was situated in the vicinity of the tricuspid valves (Fig. 4, *C*). When an attempt was made to insert the electrode into the right ventricle, the electrode curled up and was finally found lying along the auricular septum, apparently in contact with the endocardial surface. A strikingly large biphasic auricular deflection was obtained

*Since the shape of the action currents recorded from the auricles does not appear to differ fundamentally from the shape of action currents recorded from the ventricles, it seems advisable to use a comparable nomenclature. Therefore, following the standard nomenclature for QRS, the terms P_Q, P_{QS}, P_{QRS}, P_R, P_S, and P_T have been introduced to facilitate the description of the complexes obtained.

In this paper, the auricular T wave is labeled P_T, instead of T_a as has been suggested. P_T seems to be a more logical term than T_a, the derivation of which may not be readily understood.

The use of the terminology which is here proposed does not imply that the *spread* of the action current through auricular muscle is similar to the spread over the ventricular musculature.

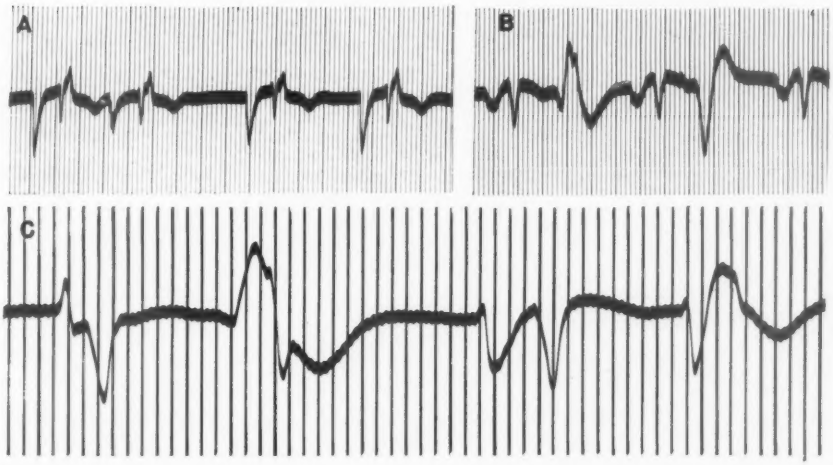

Fig. 3.—Auricular and ventricular extrasystoles. (0.5/*N* sensitivity.) *A*, Case of right bundle branch block (see Fig. 2), endocardial lead from the sinus regions. Deep P_{QS} deflections with sinus extrasystole (second beat) showing aberrant auricular response. *B*, Case of left ventricular enlargement. Upper auricular or lower superior vena cava lead. Beats 1, 3, and 5 are normal responses with deep QS deflections; Beat 2 is a left ventricular extrasystole (with large S waves in Lead I—not shown). Q wave transmitted from left ventricle, large R waves from right ventricular cavity. Beat 4 is an auricular extrasystole with abnormal P wave and a broad QS deflection (right ventricular cavity). *C*, Same case as *B*. Endocardial lead from upper auricular level. The third beat is a normal complex with a small P_R, deep P_S, and deep QS deflection. Beat 1: Auricular (nodal?) extrasystole with short P-R interval, abnormal P, and deep QS. Beat 2: Left ventricular extrasystole with large R (right ventricular cavity). The small "S wave" appears to be the final portion of a P_{QRS} superimposed upon a ventricular complex. Beat 4 represents again a left ventricular extrasystole with a P_{QRS} immediately preceding it. The early part of QRS is superimposed upon the ascending limb of P_S.

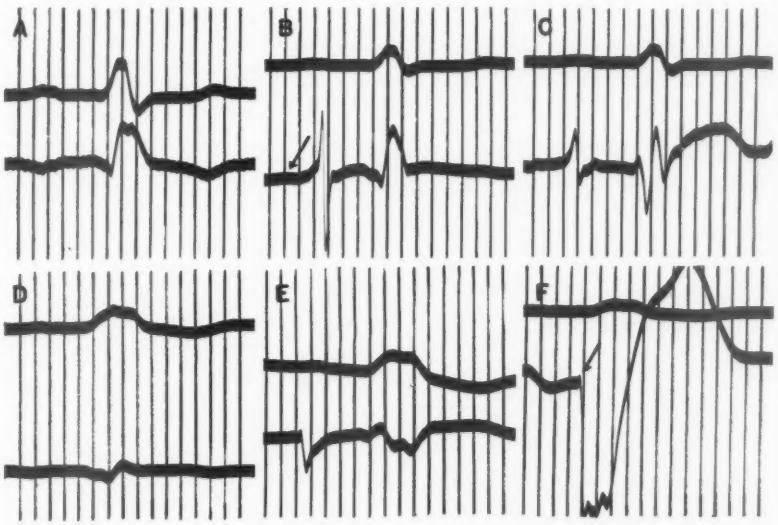

Fig. 4.—*A*, *B*, and *C*: right bundle branch block. *D*, *E*, and *F*: left bundle branch block. *A*, Lead I and V_R (2/*N* sensitivity). *B*, Lead I and electrogram from right auricle (0.9/*N* sensitivity). Arrow points to small preauricular deflection. Note P_T distorting the P-R interval. *C*, Lead I and endocardial lead from lower auricular levels (0.9/*N* sensitivity). Some distortion by artifacts. *D*, Lead I and V_R (2/*N* sensitivity). *E*, Lead I and endocardial lead from upper auricular level. Note preauricular deflection and small P_R. *F*, Lead I and endocardial lead from right ventricle (0.15/*N* sensitivity). Arrow points to small preintrinsic deflection of QRS.

which displayed a classic intrinsic deflection. Its onset appeared 0.065 second after the beginning of the auricular deflection (Fig. 4, *B*). In this case, high-speed records revealed a small, positive preauricular deflection immediately preceding the onset of P_R and occurring almost 0.05 second before the onset of P in a simultaneously recorded standard bipolar lead. A similar deflection was found in one other instance (Figs. 4, *E*, and 5, *A*).

Auricular extrasystoles showed either increased or decreased P_R deflections, when compared with the pattern of the normal beats for that region. A sinus extrasystole recorded with the electrode placed at the sinus region showed a deep but splintered P_{QS} deflection (Fig. 3, *A*).

2. *Ventricular Deflections:* Records from lower right auricular levels, taken with the electrode in the vicinity of the tricuspid valves (beneath or just to the right of the sternum), should represent potential variations of the right ventricular cavity which were transmitted through the atrioventricular opening. At higher auricular levels, the electrode is situated behind and above the ventricles and may conceivably deflect a mixture of potential variations of the right and left ventricular cavities and of endocardial action currents from both ventricles. A striking similarity was always noted between ventricular complexes recorded at high auricular levels and those recorded in a unipolar right arm lead (V_R). These records usually differed from those obtained from lower auricular or ventricular levels, particularly when bundle branch block was present (Figs. 1, 4, and 5).

The two individuals with normal ventricular activation (left ventricular enlargement) displayed deep Q-S deflections from all auricular levels, followed by small, positive T waves, often with slight elevation of the S-T segment (Figs. 1 and 3, *B* and *C*). In left bundle branch block a somewhat similar record was obtained. The QRS deflection was represented as a deep negative deflection throughout ventricular excitation, except for an earlier portion partly preceding the beginning of QRS in a simultaneously registered Lead I. The record displayed a small Q and a small R, followed by a broad and notched S (Figs. 4, *E*, and 5, *A*). The duration from the beginning of Q to the top of R measured 0.055 second; the S wave from the top of R to S-T junction, 0.125 second. The total duration of QRS in the standard limb Lead I measured only 0.165 second; in endocardial leads the duration of QRS was 0.180 second.

Records taken from the upper auricular levels of the two subjects with right bundle branch block were similar in most details to those obtained from the right arm of these subjects (Figs. 2, *A* and *B*, 3, *A*, and 4, *B*). In the first case a small R wave preceded a rapid downward deflection, after which a broad, notched R′ wave occurred which occupied more than half the total duration of QRS (Figs. 2, *A* and *B*, and 3, *A*). The small R wave was not present in a record taken from the lower auricular level, and a short but deep Q wave was noted, followed by a slightly notched R deflection. The peak of R appeared 0.04 second earlier than in upper auricular records (Fig. 2, *C*). In the second case a similar difference was noted: the record taken from the posterior aspects of the auricle was similar to V_R and displayed a small Q wave followed by a broad and notched R wave (Fig. 4, *B*). The complexes taken in the vicinity of

the tricuspid valve showed a small R, a deep S, a large R′, and a small S′. In this case, the peak of R′ occurred later than that of R in upper auricular records (Fig. 4, *C*).

Frequent ventricular extrasystoles were noted in one case. Because the extrasystoles displayed a conspicuous S wave in Lead I, they were thought to have arisen within the left ventricle. Both upper and lower right auricular records revealed large positive deflections without a trace of Q or S waves. Premature auricular extrasystoles without aberrant ventricular responses always displayed a conspicuous downward ventricular deflection (Fig. 3).

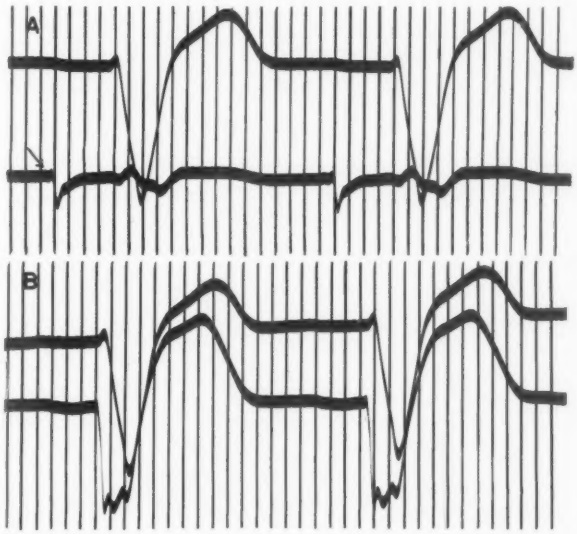

Fig. 5.—Left bundle branch block. *A*, Chest lead V_1 (0.5/N sensitivity) and endocardial lead from upper auricular level (0.5/N sensitivity). Arrow points to small preauricular deflection. *B*, Chest lead V_1 and endocardial lead from right ventricle (0.15/N sensitivity).

Right Ventricle.—In one patient with left bundle branch block, the right ventricle was entered and the tip of the electrode was found to be located to the left of the sternum, in the apical region. The voltage of QRS was about eight times higher than that observed in the auricles, while the P waves all but disappeared and became quite similar to the small, rounded deflections usually seen in standard limb leads and in precordial leads (Fig. 5, *B*). The ventricular deflections seemed to be primarily negative, but a small, diminutive R wave was noted which showed some phasic variation in height. On the average, the top of the R wave was recorded 0.003 second after the beginning of QRS. The R wave was followed by a deep and notched S deflection comprising almost the entire time of QRS. A large positive T wave followed. The downstroke of S coincided with the rise of R in a simultaneously recorded precordial lead V_1. A large, positive T wave was recorded, its peak preceding the peak of T in the precordial lead (Fig. 5, *B*). The intrinsicoid deflection (top of R) in V_1 occurred 0.022 second after the beginning of the activation of the endocardial surface. Considering the approximate thickness of the right ventricle to have been

5 mm. (slight hypertrophy) in this case, the speed of the action current through the ventricular wall would have been about 300 mm. per second.

DISCUSSION

The studies which have been presented can be regarded only as preliminary observations which need further amplification. However, some of the records which were obtained strongly support our present concepts of cardiac excitation. In this respect, three observations are of particular interest. (1) Large, predominantly negative auricular deflections are encountered at high auricular levels, and distinct P_R waves appear either when auricular extrasystoles are encountered or when the electrode is moved toward the junctional region. (2) Ventricular complexes from the junctional auricular region show negative deflections in a normally activated heart and in left bundle branch block, and show positive deflections in right bundle branch block and in left ventricular extrasystoles. (3) Ventricular complexes recorded from higher auricular levels differ from those taken at lower levels and from the right ventricular cavity. They are quite similar, however, to those which are obtained when the exploring electrode is placed on the right arm (V_R).

Auricular Activation.—The finding of an area of primary negativity in the vicinity of the opening of the superior vena cava is in keeping with Lewis' observation on the location of the cardiac pacemaker in dogs.[6] The absence of an early P_R wave is also noted in records taken from the venae cavae (Figs. 1 and 3, *B*), but the sudden and striking increase in magnitude of the deflection in the case illustrated in Fig. 2 favors the assumption that the exploring electrode must have rested close to a point which remained throughout the auricular cycle electronegative with respect to the surrounding tissue. Whatever theory is accepted, the region from which the impulse originates must always be negative to adjacent muscle. If it is assumed that the spread of the action current is characterized by a crest of positive charges immediately followed by a negative wake, the region responsible for the release of impulses must always face the electronegative wake. This region will never become positive with respect to other parts of the cardiac muscle, and an electrode placed near this region will never record a positive deflection unless the point of impulse formation has shifted. For this reason it can be assumed that the record obtained represents the potential variations of the sinus region.

A premature beat arising from this region (a sinus extrasystole) may at times find part of the auricular muscle still refractory; under these conditions an aberrant response of auricular tissue in the face of an otherwise normal activation will be obtained (Fig. 3, *A*). This should result in an abnormal P wave in standard limb leads. For standard limb leads, a sinus extrasystole is defined as a premature complex whose individual components, including P, are identical with the sinus beats. This statement should be modified, as an abnormal P might be expected to occur in standard limb leads if the new impulse falls in the recovery phase of the preceding beat. Unfortunately no simultaneous records of standard leads were made in the example shown in Fig. 3, *A*.

When the electrode is moved away from the point of primary negativity, a small P_R wave can be recorded which gradually increases in size. The preponderance of P_R over P_S increases with the distance of the exploring electrode from the sinus region. This observation favors another concept of auricular activation, which maintains that, in contrast to the manner of activation of ventricular musculature, the auricles are activated radially from the primary point of stimulation, similarly to the radial spread of waves emitted by a radio sender or by a stone thrown into a lake. The auricular electrogram which was recorded in one instance (Fig. 4, *B*) differed in no way from many experimental records obtained from isolated auricular muscle strips of the frog or turtle,[3, 4] or from the epicardial auricular records of the dog obtained in situ.[2] The similarity of the P-wave pattern in certain esophageal leads to that in auricular endocardial leads is quite striking, and was noted by Macleod and Cohn.[17] In any type of auricular muscle tissue no essential difference between endo- and epicardial records can be expected if the action current spreads radially from its point of origin. Both types of records (endocardial and esophageal) can be considered as leads taken from a simple sheet of muscle submerged in a conducting medium. The intrinsic deflection for P_R appears later in esophageal leads than in endocardial right auricular leads. This indicates merely that the distance of the exploring electrode from the point of primary negativity is greater in esophageal leads than in right auricular endocardial leads.

A small, rounded, positive deflection which definitely preceded any other evidence of auricular activation was occasionally recorded (Figs. 4, *B* and *E*, and 5, *A*). This "preauricular deflection" may be a normal constituent of the human electrocardiogram which, because of its smallness, has hitherto escaped detection in the conventional leads. Its significance is doubtful but it resembles in contour and magnitude, though not in direction, the "prepotentials" which have been recorded by Bozler under a variety of conditions. Bozler believes that these potential oscillations might initiate normal sinus discharges.[18]

Ventricular Activation.—No similarity of the electrocardiographic pattern is present when the ventricular complexes from the endocardial surfaces are compared with "epicardial" leads from the precordium or from lower esophageal levels. Deep Q-S deflections are obtained from the right auricular and ventricular cavities when conduction of impulses occurs over the intact His bundle either in normal sinus beats or in auricular extrasystoles with normal ventricular responses. This again is in agreement with Macleod and Cohn's observation,[17] and with open-chest experiments on animals where a needle electrode is thrust through the musculature into the ventricular cavities.[8] On the basis of these experiments, the characteristic Q waves of myocardial infarction have been explained as denoting the appearance of potential variations of the ventricular cavities at the epicardial surface which are transmitted through electrically inert infarcted and fibrosed areas.[9, 10, 12] The demonstration of cavity potentials of a similar kind in man makes the explanation of QRS changes associated with myocardial infarction directly applicable to human records.

The small, quite variable R wave noted at the beginning of QRS inside the right ventricular cavity in a case of left bundle branch block is of interest.

The peak of this deflection occurs 0.003 second after the beginning of ventricular excitation and precedes considerably the onset of QRS in simultaneous standard leads (Figs. 4, *F*, and 5, *B*). A small preintrinsic deflection of this kind has been previously recorded in animal electrocardiograms from the right ventricular cavity.[8, 17] In Wilson's record this deflection disappeared after left bundle branch block was produced. This experiment indicated that with a normally conducted impulse the left side of the septum was activated slightly in advance of the right. For the curves presented by Wilson, Hill, and Johnston, and also for those reported by Macleod and Cohn, this explanation appears logical and is strongly supported by reports of vector analysis of standard limb leads in human records.[19, 20] The mode of activation of the intraventricular septum apparently varies, however, and in a number of records from various animals, activation of the right ventricle was found to precede slightly that of the left.[5] In the record presented in Figs. 4, *E*, and 5, *B*, left bundle branch block was present, and activation of the septum must have occurred from right to left. Consequently the deflection cannot be ascribed to early activation of the left ventricular side of the septum. The assumption of Macleod and Cohn,[17] that R waves of this kind from the right ventricular cavity may be caused by the expanding polarization of the left ventricle after the activation of the right has been completed, appears unlikely on anatomic grounds, since it assumes that the long axis of the left ventricle exceeds that of the right to a considerable degree. At present no satisfactory explanation can be offered for this small preintrinsic deflection unless it represents activation of parts of the endocardial surface at the base of the right ventricle, and of papillary muscles. These areas are presumably activated after the activation of the apical region. The action current speeds from apex to base during the extremely short period of radial excitation of the endocardial surface; this may account for a small period of positivity similar to the much longer period of positivity found in auricular muscle.

Except for the greater width of the complexes, there is no essential difference in the activation of the right ventricle in normally activated hearts and in those displaying left bundle branch block, since polarization of the right ventricular cavity is not influenced by the altered activation of the left. The right ventricular endocardial electrocardiogram obtained in the case of left bundle branch block (Figs. 4, *E*, and 5, *B*) can be taken as representing the normal pattern of endocardial activation of the right ventricle.

The tracings obtained from cases of right bundle branch block differ essentially from those discussed before. Right bundle branch block records displayed prominent positivity during most phases of ventricular activation (Figs. 2, 3, and 4). This is to be expected if one assumes that in instances of right bundle branch block the septum and the right ventricular cavities are being activated from the left ventricle, and that therefore a layer of positive charges faces the right ventricular cavity during the major part of ventricular excitation. The occasional biphasic QRS complexes which were observed have their analogue in animal experiments. This, it seems, indicates a radial spread of the action current over the endocardial surface after the impulse has reached the right ventricular cavity through the intraventricular septum and before it assumes and completes its course through the lateral ventricular walls.

In the face of overwhelming evidence in support of the new nomenclature of bundle branch block, it need hardly be mentioned that cavity potentials of the type recorded in man in intraventricular block could be obtained only if, in records of the first type (Figs. 4, *D*, *E*, and *F*, and 5), activation is normal in the right and delayed in the left ventricle (left bundle branch block); and if, in records of the latter type, it is delayed in the right but presumably normal in the left (right bundle branch block) (Figs. 2, 3, *A*, and 4, A, *B*, and *C*). The human records which have been presented are in accord with records of certain pertinent animal experiments which have been based on the assumptions that the action currents of the heart muscle may be represented as electrical doublets, or as an electrical source followed immediately by an electrical sink, that they follow the laws which govern the flow of electrical currents in volume conductors, and that the pathways which the action current traverses are identical to those worked out over many years for various species of mammalian and nonmammalian hearts.

The Meaning of V_R.—It remains to explain the more complex ventricular records which are obtained when the exploring electrode is situated at upper auricular levels. It has been pointed out that the ventricular complexes recorded from this region are quite similar to, and sometimes identical with the so-called unipolar leads from the right arm. They differ from tracings obtained from lower auricular or ventricular levels in cases of right or left bundle branch block but are similar to records from lower auricular levels in normally activated hearts. It has been stated that the right arm potentials (V_R) represent potential variations of the ventricular cavities transmitted to this region by the large vascular openings at the base of the heart.[12, 13] It now appears that certain modification of this statement can be made. The auricular deflections in V_R are unlike the deflections in records made from the auricular endocardial surface but are similar to the deflections obtained when the electrode is located extracardially in one of the venae cavae (Fig. 1). The ventricular deflection in V_R is similar to that of endocardial records from the upper, but not from the lower auricular region. When the electrode is placed in the upper auricular position, the tip lies to the right and above both ventricular cavities and the intraventricular septum (Fig. 6, *B*). This position favors the recording of a mixture of potential variations from the basal parts of both cavities. In a normally activated heart, the potential variations of both cavities are negative, and consequently a deflection of QRS directed chiefly downward will be recorded regardless of whether the electrode records the potential variations of one or of two ventricular cavities. In left bundle branch block, the potential variations of the left ventricle are positive for the same reason that, in right bundle branch block, those in the right ventricle are positive. An electrode placed above and to the right of both ventricles will record a mixture of the positive potentials of the left and the negative potentials of the right ventricular cavity. As the right ventricle is closer to the exploring electrode, the effects of the right ventricular cavity will manifest themselves to a greater extent than those of the left, and the major portion of the electrocardiogram will show negative deflections. This preponderance of negativity will be particularly evident during the

later phase of activation, when the left ventricular cavity likewise becomes negatively charged as the impulse spreads through the lateral ventricular walls. Under these conditions a mixed record of the type obtained in Fig. 4, *E*, results. In right bundle branch block, early negative deflections with final broad R waves are typical for a right arm lead (V_R) and have likewise been recorded from upper right auricular levels (Figs. 2, 3, *A*, and 4, *A* and *B*). Again it seems likely that primary negative left ventricular potentials are responsible for the early part of QRS and that the large slurred R waves of the later phase are a reflection of the positive QRS complexes of the right ventricular cavity. Fig. 6 illustrates diagrammatically the position of the exploring electrode in relation to the potential variations of both ventricular cavities.

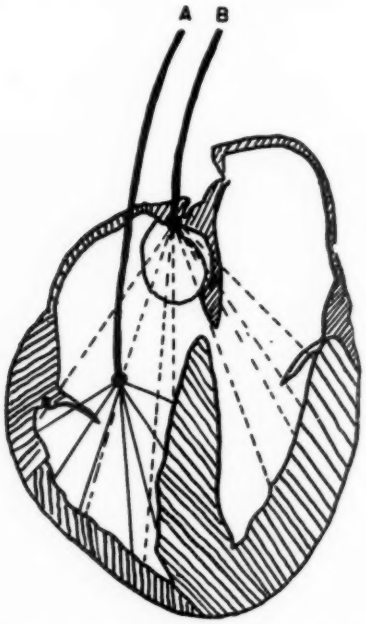

Fig. 6.—The relationship of the exploring electrode to the auricular and ventricular cavities. In position *A* the electrode is placed low in the right auricle. Position *B* is at a higher auricular level and therefore permits the recording of the potential variations of both right and left ventricular cavities (see text). The circle in the right auricle indicates the position of the inferior vena cava.

SUMMARY

1. Electrocardiograms from the endocardial surfaces of the right side of the heart and from the large veins have been obtained by means of a catheter-like electrode inserted through the right or left antecubital veins.

2. The potential variations which have been recorded are in agreement with the basic concepts of origin, spread, and distribution of the action current of the heart upon which modern electrocardiographic interpretation is based. The conclusions which have been drawn from animal experiments can safely be applied to human electrocardiography.

3. The potential variations recorded from unipolar right arm leads represent auricular deflections similar to those present in the large veins. The ventricular deflection in V_R is a faithful reproduction of records obtained from the endocardial surface of the upper portion of the right auricle. They represent a mixture of potentials from the right and left ventricular cavities.

Miss Jeanette Lelonde gave valuable assistance.

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CLINICAL PICTURE AND TREATMENT OF THE LATER STAGE OF TRENCH FOOT

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INTRODUCTION

DURING World War I, the single winter campaign in which the Ground Forces of the United States were involved resulted in approximately 2,000 cases of trench foot. In World War II, casualties of this type have been considerably greater due to the fact that a far larger Army took part in a number of winter campaigns.

A large proportion of the soldiers with trench foot have already returned to civil life, while those still in the Army will also be leaving in the near future as demobilization takes place. As a result, the burden of continuing the treatment of the sequelae of this condition will fall upon the general practitioner in civil practice as well as the physician in the Veterans' Facilities. It is, therefore, the purpose of this paper first to present the clinical picture of the patient with trench foot approximately eight months after the initial exposure and, second, to discuss the results of the various procedures that have been attempted in the later treatment of this condition. In order to evaluate the sequelae, it will be necessary, for comparison, to describe briefly the initial stages also. For the sake of simplicity in presentation, all the cases have been arbitrarily grouped into two categories, namely those without any significant loss of tissue, and those with deep gangrene.

Distinction Between Trench Foot and Other Conditions Resulting From Exposure to Cold.—Trench foot develops in soldiers compelled to remain in foxholes or trenches for a prolonged period of time during which their feet are exposed to a damp environment and to cold not necessarily low enough to freeze tissues. The almost continuous contact of the skin with water adds to the hazard of thermal injury, since as a result there is a facilitated transmission of cold to the tissues as well as an increased rate of loss of body heat. A further factor favoring tissue damage is the reduction of the circulation due to the general muscular inactivity and the cramped position in which the lower extremities through necessity must remain for relatively long intervals. Immersion foot develops in survivors of shipwrecks compelled to keep their feet constantly or intermittently immersed in cold sea water for periods of days or weeks while

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on rubber rafts or in boats. Again, the environmental temperature often ranges around 33° F. Actually, very little difference exists between this state and trench foot.

In contrast, common frostbite and high altitude frostbite follow actual freezing of tissues by exposure to sub-zero weather. High altitude frostbite develops in members of airplane crews at high altitudes, when exposure takes place either through some failure in the heating unit of the suit, or on even momentary withdrawal of an extremity from a heated glove or boot. In neither this condition nor in common frostbite does the factor of exposure to water or mud play an important role.

CLINICAL OBSERVATIONS

The data in the present report were obtained from a study of 633 patients (616 enlisted men and 17 officers) with varying degrees of trench foot, who came under observation two to thirteen months after exposure to the elements. These men remained under our care for from two to seven months and were then either returned to duty or discharged from the Army.

Patients With One or More Exposures and No Gangrene.—Of the entire series of 633 patients, 596 or 94.2 per cent had one or more distinct exposures without having developed deep gangrene on any occasion. Of this group, 526 had only one attack which was sustained in combat either in Italy in the period from November, 1943, to March, 1944, or in France, Germany, Luxembourg, Holland, or Belgium, between October, 1944, and January, 1945. The duration of exposure varied between three and fifty-four days, with an average of fourteen days. In practically all instances, the environmental temperature was around freezing or slightly above that point, and the patients were exposed to almost continuous rain. For the most part, their feet were immersed in water and mud for a number of days, without the opportunity of changing socks and shoes, except at rare intervals.

Seventy patients had had two or more attacks without developing deep gangrene. Sixty of them were exposed to the elements on two, and 10 of them on three distinct occasions. In the later instances, they sustained either a fresh case of trench foot or an exacerbation of the initial one. In the case of the patients with two attacks, the first exposure was in Italy from November, 1943, to March, 1944. The duration of the exposure was about the same as in the case of the group with a single attack, namely, an average of fifteen days, with a range of from one to sixty days. All of these patients were hospitalized for an average of nine weeks and then sent to convalescent camps or reconditioning centers, from which they were eventually assigned to duty. The second exposure in this group took place in the period between August, 1944, and February, 1945, in France, Germany, or Holland. Again these soldiers were hospitalized, but this time they remained as patients until they reached this hospital.

The 10 individuals with three exposures experienced two of these in Italy, first at Cassino and then at Anzio, and the third in France, Germany, or Holland. Following each of the first two attacks, the patients were returned to duty after

a varying period of hospitalization. With the third exposure, they were hospitalized for the last time, reaching this hospital approximately two months after the acute stage.

Patients With Deep Gangrene and Subsequent Loss of Tissue.—Only 37 patients (5.8 per cent) sustained deep gangrene of the feet with the resulting loss of tissue. This occurred after one exposure either in Italy in the period between November, 1943, and March, 1944, or in France, Germany, Belgium, or Luxembourg, between October, 1944, and January, 1945. The average period of exposure was eight days, with a range of from one to thirty-four days. All of the patients in this group were at complete bed rest when they reached this hospital approximately two to six months after the initial injury.

It is of interest to note that in both patients with and those without deep gangrene no correlation exists between the severity of the condition and the duration of exposure to the elements (Table I). Furthermore, it would appear that the individuals with an old history of frostbite or a previous attack of trench foot are no more liable to develop gangrene than are those exposed only once.

TABLE I. FREQUENCY OF LOSS OF TISSUE IN SERIES OF 633 PATIENTS AND CORRELATION WITH OTHER FACTORS

EXTENT OF PATHOLOGY	NUMBER OF CASES	% ENTIRE SERIES	AVERAGE PERIOD OF EXPOSURE (DAYS)	THOSE WITH PREVIOUS EXPOSURES (% OF GROUP)	THOSE WITH OLD HISTORY OF FROSTBITE (% OF GROUP)
Complete loss of one or both feet	1	0.1	12	0	0
Loss of toes and part of foot, both sides	2	0.3	7	0	0
Loss of toes and part of foot, one side	1	0.1	4	0	0
Entire loss of one or more toes, both feet	3	0.5	6	0	0
Entire loss of one or more toes, one foot	7	1.1	12	0	0
Loss of part of one or more toes or heel	23	3.6	7	0	10
Superficial gangrene, more extensive	33	5.3	9	0	0
Superficial gangrene, mild	15	2.4	6	0	0
No loss of tissue	548	86.6	14	12.8	7.7

Clinical Picture Shortly After Exposure.—The first symptoms experienced by most of the patients in the series were not severe or violent pains, but rather numbness, an aching sensation, intense coldness, and swelling of the feet. In some instances, the soldiers were compelled to seek medical aid after they had removed their shoes and then were unable to replace them because of the swelling. On leaving the foxhole and beginning to walk, a number of men experienced severe pins-and-needles sensations on the plantar surface of the feet.

By the time the soldiers reached a fixed installation, it could generally be determined whether or not they were going to lose any significant quantity of tissue. In those individuals who were fortunate enough to escape without any gangrene or perhaps with only involvement of the superficial layers of the skin, the feet were found to be cold, pale or cyanotic, swollen, and painful. In the

severe cases, swelling and discoloration were marked. In many of these, vesicles were present on the dorsum of the feet, which, in some instances, developed into large painful blisters containing lemon-colored or clear serous fluid. In most individuals desquamation of practically the whole sole was present, and in some this occurred a number of times. Following the loss of dead epidermis, the feet began to perspire. This generally occurred while the patients were still at bed rest, and, although minimal at the beginning, it became marked in many instances. Sweating was most often noted in the foot that was cold and cyanotic, but it was also present when the extremity was warm and of normal color.

As the patients remained in the hospital, only a small number of them demonstrated a transient period of hyperemia, as manifested by marked warmth and redness of the skin of the foot. This response subsequently disappeared and the foot became typically cold and cyanotic. The cyanosis was generally accentuated by dependency. Frequently the patients suffered from severe, burning pain, particularly at night, from which they sought relief by uncovering their feet.

For the most part the patients with deep gangrene demonstrated the same early signs and symptoms except that the clinical picture was of a more severe nature. Marked swelling, cyanosis or pallor, blister formation, severe pain in the feet, and numbness were common findings. In some instances gangrene was already present when the patient reached the Battalion Aid Station, but more often it appeared only after six to ten days of hospitalization. At times the gangrene was preceded by large hemorrhagic blisters. The involved areas quickly became black and mummified. In some individuals ulcerated sites were present; above these the tissues showed signs of inflammation. In others complicating infection already existed.

It is not within the scope of this paper to discuss treatment during the early stage of trench foot. From a review of the records of the patients studied, it is difficult to assay with any degree of accuracy the relative worth of the various measures which had been initiated.

SEQUELAE

Manifestations of the later stage of trench foot, as studied in this hospital, can grossly be divided into three general categories. One group of patients demonstrated signs suggestive of excessive sympathetic activity, but had minimal complaints. Another group had symptoms referable to involvement of peripheral nerves, but showed few objective findings. The patients in the third group displayed both subjective and objective clinical manifestations.

Patients With Predominant Signs of Excessive Sympathetic Activity.—Of the entire group of patients, 144 (22.8 per cent) demonstrated findings which were primarily the result of excessive sympathetic activity. The skin temperature of the toes was found to be low; frequently lower than the environmental temperature. Hyperhidrosis also was present, varying from slightly greater than normal to the point where the sweat rolled off the foot almost in a continuous flow. The quantity of perspiration was definitely increased by emotional

factors. The fact that the skin temperature was lower than the environmental temperature was due to the cooling effect produced by the evaporation of perspiration. Cyanosis of the feet, particularly in the dependent position, was also a prominent finding in this group.

A number of patients would occasionally show a change from a blue, cold foot to a red, hot one. This effect could be produced by exposing the extremities to a warm room or, in some instances, by walking a short distance with shoes on. At other times, for no apparent reason, the foot would become red and hot, and then revert to a cold state. Mottling of the skin was a fairly common finding. In some patients this was only a transient phenomenon, while in others it remained for a relatively long period of time. Various types of patterns were present, occasionally in the same individual. For the most part the mottling was produced by sharply demarcated areas of rubor on a background of cyanosis, interspersed with patches of pallor.

Examination of the large peripheral vessels in the patients with no deep gangrene revealed the absence of the dorsalis pedis artery, either on one side or both, in about 6 per cent of cases (Table II). Whether or not this finding had any significance is difficult to state since comparable results have been noted in groups of normal soldiers. No signs of arteriosclerosis were observed in any of the patients in the series. In the case of the individuals with deep gangrene, the dorsalis pedis artery was not palpable in those instances in which the process had extended onto the dorsum of the foot. Similarly, in one instance, the posterior tibial artery could not be felt. A history of intermittent claudication was obtained only infrequently, thus suggesting that for the most part there was no impairment of the blood supply to the muscles of the legs.

TABLE II. MANIFESTATIONS FOUR TO THIRTEEN MONTHS AFTER EXPOSURE IN A SERIES OF 596 PATIENTS WITHOUT GANGRENE

SIGNS	FREQUENCY %	SYMPTOMS	FREQUENCY %
Cyanosis	59.1	Aching	3.8
Absent pulsations, large arteries	6.0	Tenderness in sole of foot	13.6
Sweating	50.4	Numbness	16.6
Abnormal gait	34.0	Neuritic pains	14.3
Atrophy of muscles	14.7	Hypesthesia	41.5
Stiffness of toes	10.0	Burning and tingling	21.9
Coldness	27.9		
Edema	17.4		

Oscillometric readings were performed on the first 40 patients examined, and no significant alterations were observed. The effect of indirect vasodilatation, brought about by applying hot-water bags to the abdomen and chest and covering the subject with a number of woolen blankets, was studied on 25 subjects. In all instances, this procedure brought the skin temperature, which was low at the beginning, to a level considered to be normal under these circumstances. In 11 cases, a paravertebral lumbar sympathetic block with procaine was done and a similar type of skin temperature response was obtained. With

the rise in the skin temperature, the cyanosis of the foot was replaced by rubor and the hyperhidrosis disappeared entirely for a short period.

In 10 patients with cyanosis but no deep gangrene, the reactive hyperemia test[1] was performed. In all individuals the flush, which appeared on removal of the pressure in the cuff, spread over the leg within five seconds and involved the toes maximally in ten seconds. The flush faded out in about one to two minutes. The rapidity of the response indicated a normal reaction of the cutaneous arterioles and small vessels (capillaries and subpapillary venous plexuses) to a period of anoxia and helped to rule out the presence of occlusive vascular disease in these vessels.

The above tests substantiated the view that the late findings in this group were due primarily to excessive sympathetic activity rather than to organic involvement of the blood vessels of the lower extremities.

Patients With Manifestations Referable to Peripheral Nerve Involvement.—The second category included 63 patients (9.9 per cent) in whom the signs and symptoms were suggestive primarily of some type of peripheral nerve involvement. Objectively there were frequently very few abnormalities noted. The main complaint was tenderness over the metatarsophalangeal portion of the foot, which at times was of such a degree that the patients did not allow even the slightest pressure to this part. As a result, some of them were unable to walk at all, or, when they did, they placed their weight on the heel or along the lateral edge of the foot. Many of these individuals were found to have areas of hypesthesia to pinprick and cotton wool, which corresponded closely to the sites which were sensitive to deep pressure. The hypesthesia sometimes involved the plantar and even dorsal surfaces of the toes and the dorsum of the foot. Anesthesia was rarely present. In some individuals hyperesthesia was a disturbing symptom. Sensation in the legs was only infrequently altered.

The patients in this group also complained of various types of paresthesias, such as burning and stinging sensation and a pins-and-needles sensation in the toes. Furthermore, they described shooting pains in the feet, which appeared while at rest, and a sensation of numbness in some of the toes.

Patients With Both Syndromes.—The third and largest group consisted of 426 cases (67.3 per cent) showing signs and symptoms of both excessive sympathetic activity and some type of peripheral nerve involvement. Besides these findings, many of the patients in this category, as well as in the other two, entered the hospital still showing the presence of considerable desquamating, thick epidermis on the plantar surfaces of the feet (Fig. 1). This material gradually fell off, leaving new, thin skin. Marked swelling of the toes and, to a less extent, of the feet was present in 28 patients (Fig. 2).

The presence of atrophy of the small muscles of the foot, giving the appearance of an abnormally high arch, was observed to some degree in most of the individuals and was quite marked in 26 patients. It was difficult to determine whether the response was a nonspecific effect due to disuse or whether it was part of the pathology of the trench foot syndrome. However, the existence of histologic alterations in the muscles and nerves in the initial phase of this con-

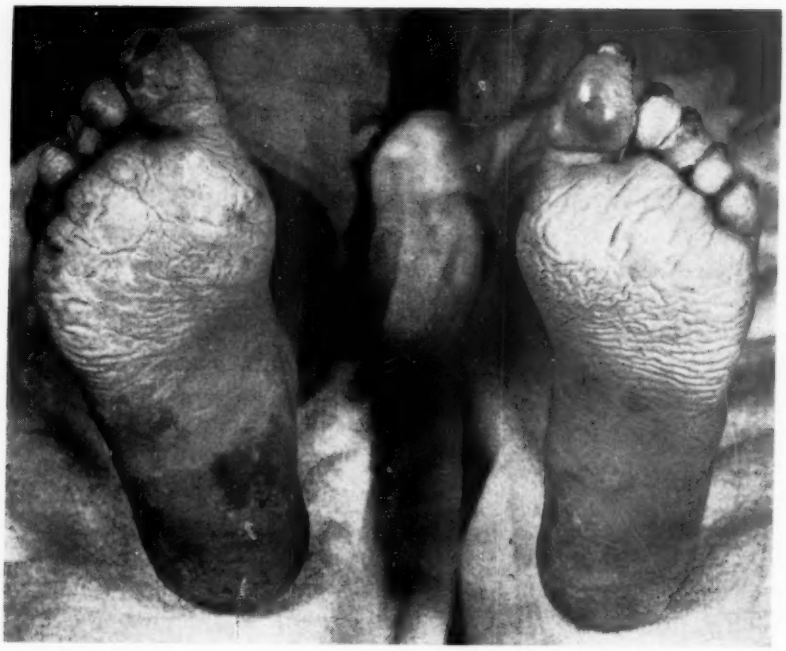


Fig. 1.—Typical case of hyperkeratosis of the skin three months after exposure to snow and cold, wet weather for three days. Skin wrinkled and fissured, similar to type of response seen after long immersion of tissues in water. Dry gangrene at tips of toes. Normal pulsations in peripheral arteries.

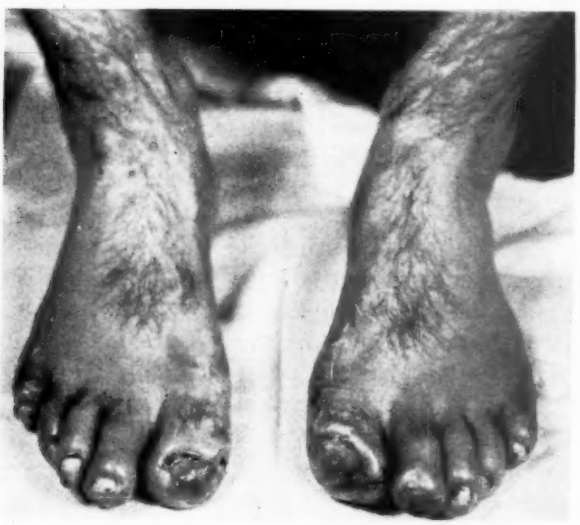


Fig. 2.—Persistent swelling of feet and presence of gangrene four months after exposure to the elements for eight days. Granulating wounds of both great toes present and also some infection.

dition[2] favors the latter view. In some instances, in spite of an intensive and prolonged program of exercises utilizing the small muscles of the foot, these patients showed no beneficial effects and, at the time of discharge from the hospital, considerable atrophy still existed.

Osteoporosis of the bones of the feet was a fairly common finding in the more severe cases. This may also have been either a response to the long period of inactivity or part of the trench foot syndrome. In several instances, the process was no longer present at the end of the period of hospitalization. More frequently, however, very little change was observed in the final film after two to three months of physical activity. Whether or not this change is ordinarily an irreversible one can only be determined by follow-up studies on such a group.

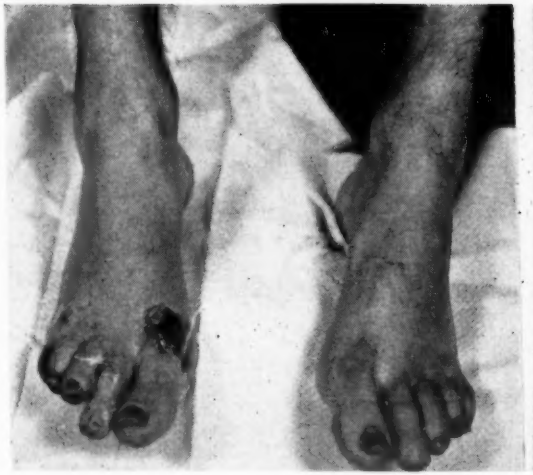
Among the patients with one or more exposures and no deep gangrene, there were 48 who entered this hospital still showing areas of superficial gangrene. These were generally present on pressure points in contact with the shoe, such as the medial aspects of the feet (Fig. 3, *A*), the tips of the toes, and occasionally the heels. For the most part, the gangrenous material separated spontaneously, leaving exposed a thin, tightly drawn, smooth, shiny skin which gradually resumed a normal appearance (Fig. 3, *B*). It is of interest that in a number of these patients the original description of the lesions would have supported the belief that a much more severe type of involvement existed than was substantiated by subsequent events. Such findings are in accord with the view that conservatism should be practiced in the early treatment of gangrene of the feet in trench foot.

Practically none of the patients showed vesicles at this stage of the disease. Frequently one or more toenails had fallen off, leaving the nail bed exposed; or the nails were distorted with a considerable amount of debris beneath them. Dermatophytosis was a common finding in this group.

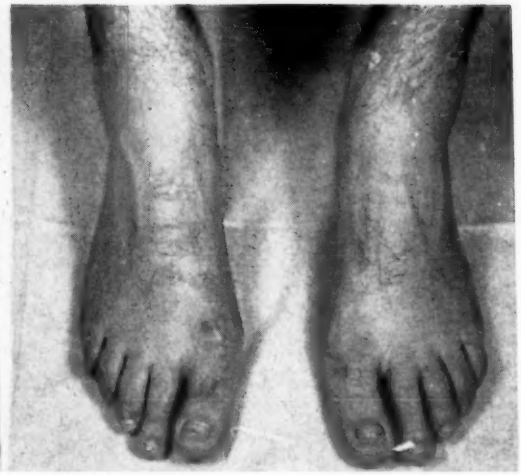
Forty-two of the patients demonstrated marked stiffness of the toes with a shiny, firmly attached skin. In some individuals, the great toe was widely separated from the others (Fig. 4) and was either hyperextended (in the form of a pseudo Babinski sign) or flexed. These observations have been previously described by other investigators.[3] There was no correlation between the degree of stiffness and the severity of the condition originally, and it was felt that this response was probably due in great part to disuse.

With regard to the group of 37 patients with deep and extensive gangrene, frequently the gangrenous portions were partially separated at the line of demarcation at the time of admission to the hospital. The lesion was generally bathed in foul-smelling pus and in some instances there was evidence of extensive infection throughout the gangrenous portions. On numerous occasions, where the gangrene appeared to be of a dry type, removal of this material through the line of demarcation disclosed a pool of pus beneath it.

Infection was invariably a mixed one and very commonly penicillin- and sulfonamide-resistant *Bacillus proteus* and *Bacillus pyocyaneus* were present. There was little spread of the infection to the adjacent soft tissues, but osteomyelitis was frequently noted in the proximal stump.



A.



B.

Fig. 3.

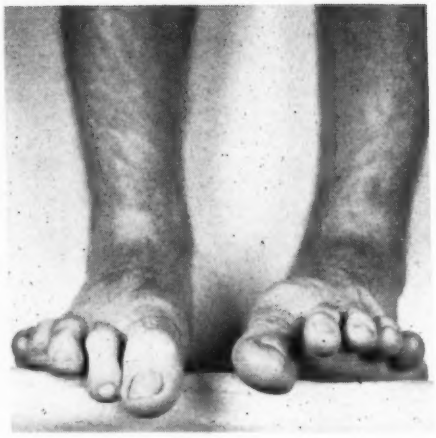


Fig. 4.

Fig. 3.—*A*, Superficial gangrene on medial aspect of right foot and some deep gangrene at tips of toes still present two months after exposure. *B*, Two months later. Superficial gangrenous area completely healed, leaving only some pigment deposits in involved site. Loss of nails on a number of toes.

Fig. 4.—Characteristic position of great toe of left foot and stiffness of toes nine months after onset of condition.

LATER THERAPY

Most of the patients with trench foot arriving at this hospital had been at complete bed rest without latrine privileges for from one to twenty weeks, with an average of nine weeks. Therefore, the treatment, whenever possible, was directed at making them ambulatory as rapidly as their condition permitted. The problem of reconditioning was made more difficult by the fact that many of the men still had considerable tenderness of the soles of the feet, pain, and swelling. All these factors made the resumption of walking an unpleasant experience. Therapy, therefore, was divided into two periods, namely, the medical and surgical treatment, followed by the reconditioning program.

MEDICAL AND SURGICAL TREATMENT

Massage and Removal of Dead Epidermis.—Most of the patients showed the presence of a considerable amount of desquamating epidermis (Fig. 1), which was removed by rubbing lanolin ointment, containing 4 per cent salicylic acid, into the skin. The procedure was performed by the patient at frequent and scheduled intervals during the day, under the supervision of a physical therapist. When desquamation was completed, the ointment was replaced by mineral oil and a dilute solution of alcohol for the purpose of massage. This step was carried out at least twice daily for half-hour intervals either by the patient himself or by the patient in the next bed. Considerable emphasis was also placed on the practice of active manipulation of the toes in order to counteract the stiffness, contractures, and atrophy of disuse. In some instances where these findings were quite marked, the daily routine of massage was supplemented by passive and active exercise of the toes by the physical therapist.

Typhoid Vaccine.—When patients with trench foot were first received at this hospital, an attempt was made to determine the effect of typhoid vaccine on the condition. A number of subjects picked at random were given this treatment; after a series of 10 to 15 intravenous injections every other day, the results were analyzed. Preliminary testings were done on each patient and the dosage of the vaccine was increased to the point where a single injection was followed by a rise in body temperature to approximately 102° F.

For the most part, this treatment brought about no definite change in the clinical picture, except for a significant reduction in the swelling of the feet in some instances. Typhoid vaccine was, therefore, subsequently utilized only in those patients in whom edema was the main complaint. In 10 of 16 individuals, there was a rapid subsidence of the swelling after the first or second administration, and the therapeutic effect continued but was less marked with the following 10 to 12 injections. At the end of the period, all of these patients were fully ambulatory, whereas previously they had been compelled to lie in bed a considerable portion of the day because of the swelling. It is of interest that complete bed rest for a number of weeks before this treatment had been started had produced little change in the edema. In the remaining six patients, typhoid vaccine did not have any therapeutic effect.

It would appear, therefore, that this treatment has some promise and that it should at least be tried in the case of every patient with trench foot who has appreciable swelling of the feet. Whether or not it will have any effect can be readily determined after the second or third injection.

Orthopedic Appliances.—As soon as the patient without gangrene was physically able, he got out of bed and began to walk, using low shoes. It was felt that these would be more satisfactory than the garrison shoes because of their light weight and because less of the foot was covered, thus permitting greater evaporation of perspiration. In patients in whom hyperhidrosis was a prominent symptom, the shoes were perforated in a number of sites, to facilitate removal of the excessive perspiration by air currents.

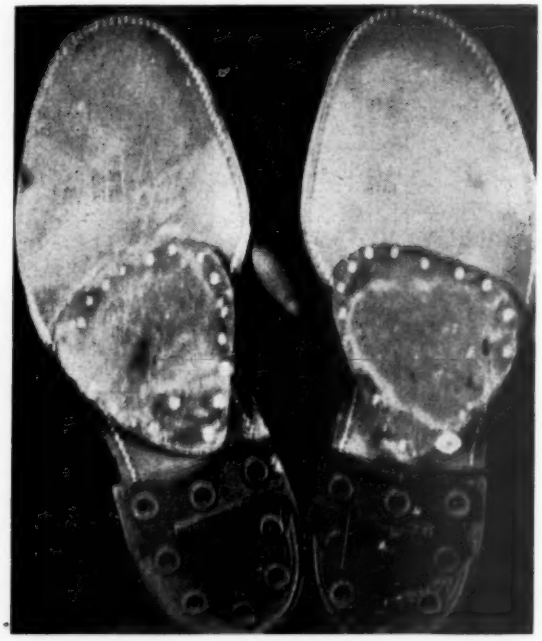


Fig. 5.—Application of anterior heel in front of normal heel, to remove pressure from sole of foot.

At least 182 of the patients without gangrene complained of tenderness over the distal portion of the foot on the plantar surface. In an attempt to protect this area from the weight of the body, these individuals, on walking, shifted the pressure to the heel or to the lateral edge of the foot. In order to counteract these unnatural gaits, with their resulting undesirable alterations in the dynamics of the foot and spine, a rubber heel or a thick piece of leather was attached to the under surface of the shoe in front of the ordinary heel* (Fig. 5). The patient then walked on the two heels, thus applying practically no pressure to the sole of the shoe which covered the sensitive portion of the foot. As he continued to walk, the anterior heel which received most of the friction

*The authors are indebted to Captain R. Buck at whose suggestion this procedure was given a clinical trial.

gradually wore down, until eventually the pressure was again applied to the sole of the shoe. In most instances, the sensitivity of the foot to pressure was lost or diminished by this time and the heel was removed.

Formalin by Iontophoresis.—Since hyperhidrosis was a common and, at times, incapacitating complaint, attempts were made to treat it, generally without too much success. Low shoes, daily foot baths, foot powders, and frequent changes of socks only partially counteracted this condition.

At the suggestion of Freis,[4] patients with severe hyperhidrosis were treated with formalin by iontophoresis. The use of formalin baths for hyperhidrosis has been a fairly common therapeutic procedure in the field of dermatology and it was felt that this action could be accentuated by forcing the formalin into the skin by means of a galvanic current. A description of the procedure we used to accomplish this follows.

An ordinary galvanic current machine was connected to the patient by placing a large negative electrode in close contact with the abdomen, while the positive electrode was immersed in a bakelite container filled with 1 per cent formalin. The patient placed both feet in the basin, which was filled with sufficient solution to reach above the ankles. Ten to 12 milliamperes of current were applied for twenty minutes. A series of treatments consisted of six daily administrations.

In all instances the patients were first skin tested for formalin sensitivity. No patient who showed even the slightest reaction was given this treatment. The presence of sensitivity to formalin appears to be fairly common, as indicated by the finding that approximately 28 per cent of all the individuals tested showed a positive reaction.

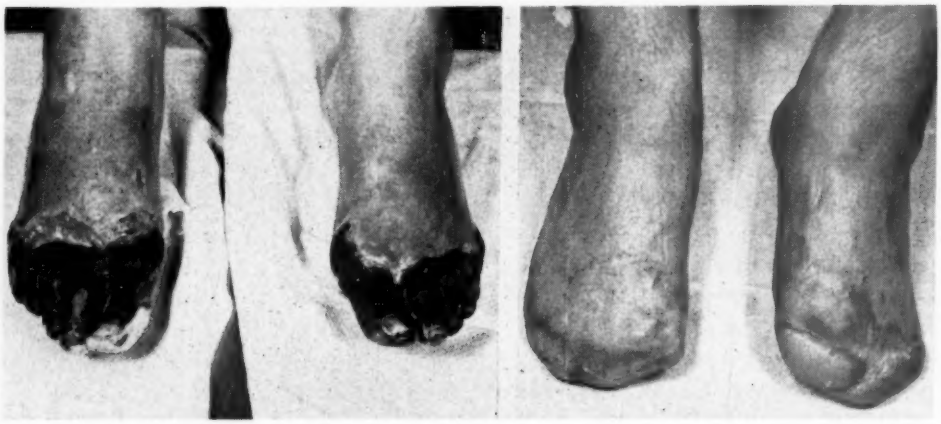
Results with formalin by iontophoresis were rather variable. The therapy was begun on 121 patients, but in 29 instances it had to be discontinued after the second or third treatment because of the appearance of a mild dermatitis or fissuring of the skin between the toes. Of the remaining 92 patients, 74 finished one series of six treatments, while 18 were given two series, with an average of thirty-nine days between treatments. In the case of the patients given one series of treatments, 37 showed an almost immediate cessation of sweating, 21 had a fair response, and 16 demonstrated no benefits from the therapy. The patients were re-examined at the end of a four-week period, and, at that time, it was felt that in seven the therapeutic effect was excellent, in 32, good, in 16, fair, and in 19, poor.

Eighteen patients were given a second series of treatments either because no therapeutic effect was noted initially or because the reduction or cessation in sweating was only temporary. In this group, the second series produced a good result in six, a fair response in eight, and a poor result in four patients.

All of the patients discussed were seen at intervals during the subsequent two months, and it was noted that in the great majority of them hyperhidrosis was returning, but generally not to the same degree as previously. The therapy evidently has a definite but transient effect on reducing sweating of the feet in trench foot.

Lumbar Sympathectomy (Table III).—Since vasoconstriction is one of the fundamental factors in the pathogenesis of trench foot and also one of the most constant sequelae, the use of sympathectomy as a possible therapeutic aid has been proposed and has received some clinical trial. This procedure was therefore utilized in a number of individuals in this series.* In nine patients the operation was done primarily for cold sensitivity or excessive hyperhidrosis, with the result that the feet became warm, dry, and normal in color. In two instances in which maceration of the skin and infection had been present, these findings cleared up shortly after sympathectomy. In all nine patients the abnormal response to cold and the associated discomfort were also minimized.

In 10 individuals in whom sympathectomy was performed primarily because of pain on weight bearing, the results were variable. Two patients with pain both in the metatarsal region and in the heels experienced complete relief in the latter site only, while those with symptoms in the metatarsal region alone were for the most part not benefited by the procedure. Somewhat similar results have been reported by Edwards, Shapiro, and Ruffin.[6] Sympathectomy was also used in a group of patients with deep gangrene, and the results in this type of case will be discussed in the section following.



A. *B.*

Fig. 6.—*A*, Deep gangrene of toes of both feet two months after exposure to snow and cold, wet weather for six days. Areas of dry gangrene demarcated from normal tissue. Foul-smelling discharge present from these sites. Normal oscillometric readings and normal pulsations in large arteries of feet. *B*, Complete healing two months later, following sympathectomy, amputation of gangrenous toes and, subsequently, pedicle transfer grafts.

Treatment of Extremities With Deep Gangrene.—In only one of the patients with deep gangrene had any surgical procedure been performed before admission to our hospital. In all others, steps had to be carried out to remove the gangrenous material (Fig. 6). In order to facilitate healing, sympathectomy was performed as a preliminary step in 30 patients; in eight of these, the procedure was done bilaterally (Fig. 6). Frequently, removal of gangrenous material and portions of toes was carried out at the same time. Twenty-nine

*A detailed analysis of the efficacy and limitations of sympathectomy has been reported in a separate paper.[5]

TABLE III. INDICATIONS FOR USE OF LUMBAR SYMPATHECTOMY

CONDITION	RESULTS	REMARKS
Hyperhidrosis alone	Complete cessation of sweating	Operation generally not indicated for this state alone
Hyperhidrosis with maceration of skin and secondary infection	Complete cessation of sweating with healing of skin	Operation definitely indicated
Marked cyanosis and coldness and abnormal response to low environmental temperature	Return of normal color and skin temperature	Operation indicated in some instances
Tenderness of sole of foot on walking	Only occasionally effective	Operation not performed for this condition alone
Neuritic manifestations	Only occasionally effective	Operation not performed for this condition alone
Deep gangrene requiring amputation and skin graft	Aids in healing	Necessary preliminary step in many cases

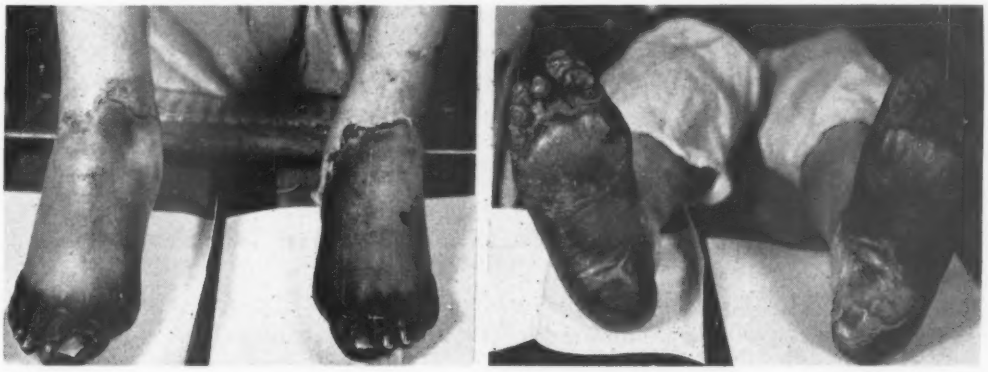


Fig. 7.—Marked gangrene involving entire foot bilaterally, one month after exposure to snow and cold, wet weather for thirteen days. Both feet subsequently amputated.

amputations were performed, and in each instance conservatism with regard to the amount of tissue removed was practiced. Nine patients required split-thickness skin grafts. In two cases, in which ends of metatarsal bones were exposed with large skin defects, it was necessary to utilize pedicle transfer grafts from the opposite lower extremity in order to obtain well-padded, full-thickness skin (Fig. 6, *B*). One patient with gangrene of both feet was sent to an amputation center for further treatment (Fig. 7).

When the patients became ambulatory again, they were fitted with special shoes to help overcome the difficulty produced by loss of tissues of the foot. In most individuals in this group, however, very little was required since a useful foot remained.

With respect to the evaluation of sympathectomy in the treatment of gangrene, it must be pointed out that no control series of cases was run simultaneously. Hence, there is no unequivocal evidence that the rate of healing was affected by the procedure. Nevertheless, there was some indication that the increase in circulation which followed had a beneficial effect in those instances in which marked vasospasm was present.

With regard to the use of split-thickness skin grafts and transfer pedicle grafts, there is little question that these procedures definitely reduced the period of invalidism. Furthermore, as a result, a thick layer of skin which responded well to the application of pressure and friction now covered the stump (Fig. 6, *B*) instead of the usual thin, poorly nourished skin which would have followed as a natural course.*

Therapeutic Procedures of Questionable Value.—A certain number of therapeutic procedures were attempted with little hope that they would prove efficacious. As anticipated, the results were for the most part unsatisfactory. However, the data will be presented, so as to discourage further clinical trials of these medications by other workers.

Four patients with marked signs of excessive sympathetic tonus were given a series of six daily treatments with mecholyl (acetyl-beta-methyl-choline chloride) by iontophoresis. The procedure was similar to that used in the case of formalin by iontophoresis (discussed previously), except that a 0.2 per cent aqueous solution of mecholyl was utilized instead of formalin. It was felt that since mecholyl by iontophoresis is a good local vasodilating agent,[7] the procedure might help in counteracting the vasospasm which existed in the patients in this group. In each instance the feet became warm for a short period following the treatment, but then reverted to the previous cold, blue state. At the end of the series of treatments, no permanent effect on the condition of the blood vessels was noted in any of the patients and the method was therefore discontinued.

In 11 patients with predominantly peripheral nerve involvement, the effect of large doses of thiamine chloride administered intravenously was studied. Each patient was given 100 mg. of the drug daily for an average of two weeks. No untoward effects were noted following the treatment, and similarly no alteration in symptoms occurred. The patients continued to complain of paresthesias, aching and burning, and sensitivity in the soles of the feet. No data were obtained from the study which would suggest that this type of therapy was at all worth while in the treatment of the neuritic complaints present in the later stage of trench foot.

The effect of Buerger's exercises and Sanders' bed was studied in eight patients with moderately severe trench foot but no gangrene. No obvious alteration was noted in such signs as cyanosis, coldness, or hyperhidrosis; nor was there any reduction in the severity of the symptoms.

In 11 patients, paravertebral lumbar sympathetic blocks were performed. As mentioned previously, this was carried out to determine whether or not the cyanosis, coldness, and hyperhidrosis were due to excessive sympathetic tone. At the same time, an opportunity was afforded to study the therapeutic effect of such a procedure. In five instances, the symptoms were unchanged. The tenderness over the sole of the foot, the swelling, and the neuritic pains were not affected. However, in the remaining six patients, some alleviation of the sensitivity of the sole of the foot resulted, but this lasted for only a short period

*A detailed analysis of the surgical management of gangrene in trench foot will be reported in a separate publication.

of time. It is of interest that, when a number of these were subsequently sympathectomized, the therapeutic effect was much less than anticipated on the basis of the findings following the block.

RECONDITIONING PROGRAM

A number of patients with trench foot did not immediately become ambulatory on reaching the hospital either because of the presence of gangrene or infection or because there was marked sensitivity of the soles of the feet which did not permit weight bearing. A special type of reconditioning program was therefore instituted to take care of these individuals during the period that they were compelled to remain in bed in order to prepare them for the time when they could participate in more active physical exercise. The routine consisted of morning corrective exercise in bed and afternoon sessions of games, tournaments, and various types of physical fitness testing.

As soon as the patients were able to walk around the ward without too much difficulty, they were started on an ambulatory reconditioning program which for the first four weeks consisted of exercises requiring them to be on their feet only a small portion of the time. During the second four-week period, this was gradually increased until the desired level of activity was reached. Then it was maintained for varying periods of time ranging from another month to three months, depending upon the rate of progress of the individual patient.

The men were given various types of rather strenuous calisthenics in a pool, since it was felt that under these circumstances the buoyancy of the water would permit more vigorous use of the muscles of the feet with less associated pain and would also help in the recovery of a sense of balance. Except for an occasional individual who responded poorly to immersion of the feet in water, the men participating in this part of the program appeared to benefit from the exercises.

At the same time, the patients were encouraged to ride a bicycle since this sport helped to improve the tone and the strength of muscles of the lower extremities. Group walking at a leisurely pace was also an important part of the program. The distance covered was gradually increased until it consisted of from 1 to 2 miles. The main purpose was to accelerate the rate at which toughening of the skin on the soles of the feet was taking place.

Results With Reconditioning Program.—The first therapeutic effect from the reconditioning program was a rapid change in the mental outlook of the trench foot patient. Having led a life which was very similar to that of a bedridden invalid for the previous two to three months, he suddenly found himself part of a program of gradually increasing physical activity. He began to do things which he did not believe he would ever be capable of performing again, and gradually, as his general physical condition improved, his self-confidence also returned. Constant participation in competitive sports helped change his attitude toward future duties and responsibilities.

When it was felt that the patient with trench foot had obtained maximal benefit from reconditioning with respect to his general health, and that his feet were sufficiently recovered to allow taking part in a fairly normal program of daily physical activity, hospitalization was terminated.

FINDINGS AT FINAL EXAMINATION

Except for 51 men who were transferred to convalescent centers or to other hospitals, the patients were sent either to a limited type of duty or were discharged to civilian life. The factors which were taken into consideration before a decision was reached were the severity of the signs and symptoms that still persisted, the rate of progress of the case in the hospital, the period of total hospitalization, the mental outlook of the patient, and the presence of multiple defects. Among the signs and symptoms, the ones that were given special attention were: the type of gait, the degree of hyperhidrosis, the presence of atrophy of the small muscles of the feet, the actual loss of tissue as a result of gangrene, the distance the patient was able to walk without difficulty, the tendency toward blister formation and fissures, the state of the skin on the soles of the feet, and such complaints as paresthesias and tenderness of the soles of the feet.

Patients Returned to Duty.—In the case of the group returned to duty (33 per cent of the series), most of the men were able to walk without difficulty for at least a mile and they all had a normal gait, placing the pressure properly on the entire foot. They were also able to stand on the distal part of their feet and elevate the heels from the ground. There were no signs of excessive sweating, coldness, atrophy of the small muscles of the feet, or stiffness of the toes. Cyanosis was minimal. There were very few complaints of paresthesias, numbness of the toes, or tenderness of the soles of the feet on walking. These patients had no other medical or surgical conditions, including any type of wound with residuals. During their period of hospitalization, they had shown fairly rapid progress.

Patients Discharged to Civilian Life.—In the case of the patients discharged from the hospital to civilian life (67 per cent of the series), approximately one-third had an associated condition or conditions which by themselves might not have been disabling, but together with a moderate degree of trench foot were sufficient to necessitate discharge from the Army. These medical defects consisted chiefly of a mild-to-moderate degree of psychoneurosis, plantar warts, various orthopedic conditions of the feet, and partially disabling wounds of the lower extremities.

In most instances, these patients did not have a normal gait even after four to eight months following their initial exposure. They either walked on their heels, on the lateral edges of the feet, or kept the toes extended so that they did not participate in weight bearing or propulsion. All of them complained of the inability to walk more than ½ mile without developing severe aching and burning in the feet. Many of the patients still demonstrated an annoying hyperhidrosis, which required changing socks as often as two or three times a day, and other findings indicating excessive sympathetic activity, such as cold, cyanotic feet. Exaggeration of symptoms, particularly in the case of sweating and swelling of the feet, was frequently noted during hot weather. Some of the patients described a neuritic type of pain at rest and also numbness of one

or more toes. Occasionally hypesthesia on the plantar surfaces of the toes and adjoining portion of the foot was still present. For the most part, the skin on the sole of the foot was delicate, probably because the patients in this group walked very little, in order to minimize the associated pain.

Except for two patients with minor lesions and good recovery and one who was transferred to an amputation center, all others with a history of deep gangrene and subsequent loss of tissue were also included in this group. Most of them had experienced a severe attack of trench foot and at the time of their disposition still displayed such sequelae as hyperhidrosis, extreme coldness and cyanosis of the feet, and manifestations of definite neuritic involvement, besides the loss of toes or portions of the feet.

FOLLOW-UP STUDIES

Recently a questionnaire was sent to the first 250 patients in the group returned to civilian life for the purpose of obtaining information concerning their progress in the interval. One hundred eighty-eight replies were received, and the data have been analyzed. It is intended to continue this study at three- to six-month periods in order to determine the residuals of trench foot which persist, and whether or not individuals with this condition become useful members of their community again.

From an examination of the questionnaires, it was found that 68.3 per cent of the patients obtained jobs within an average of 4.2 weeks after being discharged from the Army. Four per cent enrolled for courses in technical schools and colleges, while 27.7 per cent had no job at the time of filling out the questionnaire (approximately two and one-half months after they had left the hospital). Forty-nine per cent of those who were working still had the job they originally obtained. Thirty-two per cent of the entire group, including those without jobs at present, had to change positions from one to three times. As will be noted in Table IV, *A*, a great proportion of the men had jobs requiring physical labor, while only a small number were doing a sedentary type of work. For the group as a whole, the men spent an average of four hours on their

TABLE IV. EVALUATION OF PROGRESS OF PATIENTS APPROXIMATELY THREE MONTHS AFTER RETURN TO CIVILIAN LIFE

A. Types of Occupation

TYPE	% OF CASES	TYPE	% OF CASES
Farming and gardening	15.4	Factory worker	30.5
Cab or truck driving	14.6	White-collar job	24.0
Machinist or helper	15.5		

B. Symptoms Which Persist in the Feet

SYMPTOMS	% OF CASES	SYMPTOMS	% OF CASES
Burning sensation	72	Tenderness, sole of foot	69
Hyperhidrosis	63	Dermatophytosis	28
Blister formation	26	Swelling	59

C. Ability to Walk

DISTANCE	% OF CASES	DISTANCE	% OF CASES
Less than ¼ mile	12.9	¾ mile	8.7
¼ mile	12.1	1 to 1½ miles	33.7
½ mile	17.2	2 to 3 miles	15.4

feet daily. Twenty-two per cent of them were able to do their job as well as the man working next to them who had no physical disability, while 78 per cent were not.

With respect to their medical status, a great proportion of the patients still had numerous complaints (Table IV, *B*). Their ability to walk ranged from less than ¼ mile to as much as 2 or 3 miles (Table IV, *C*). Forty-seven per cent of the patients stated that they had observed no improvement in their condition since they had left the hospital, 43 per cent noted slight improvement, and 10 per cent noted more marked improvement.

SUMMARY AND CONCLUSIONS

1. The later sequelae of trench foot were studied in a series of 633 soldiers with varying degrees of involvement of the feet.

2. Ninety-four and two-tenths per cent of the patients had one or more exposures but never developed gangrene.

3. Five and eight-tenths per cent of the patients developed gangrene with the loss of deep tissues of the feet.

4. No apparent correlation could be obtained between the duration of the initial exposure and the severity and persistence of the condition. Similarly, there was no tendency for the patients with a history of frostbite to develop a more severe case of trench foot.

5. Shortly after exposure, the feet were swollen and discolored and showed vesicle formation, desquamation of the sole, and hyperhidrosis. Such complaints as pain, numbness, and paresthesias were frequently present.

6. The sequelae of trench foot were divided into three groups, of which one demonstrated findings indicating excessive sympathetic activity, the second, a clinical picture suggestive of some type of peripheral nerve involvement, and the third, signs and symptoms common to both of the other two groups.

7. Various tests were performed on the group of patients with signs of excessive sympathetic activity but without gangrene. These procedures supported the view that no occlusive vascular disease was present in the later stage of uncomplicated trench foot.

8. Frequently, no correlation could be made between objective findings and complaints experienced by the patient. In some cases, practically no signs of excessive vasomotor tonus were present, and the feet looked normal on inspection; still the patients walked on their heels or along the lateral borders of their feet, because of tenderness in the soles. They also had various types of paresthesias. On the other hand, some individuals showed signs of excessive sympathetic activity, such as cold, wet, cyanotic feet, or they even had superficial gangrene, without any indication of nerve involvement. Their gait was normal; many of them were able to walk a mile or two without experiencing any discomfort.

9. The treatment of the sequelae of trench foot was divided into two categories, namely, medical and surgical therapy and the reconditioning program. The medical and surgical treatment was directed toward removal of the dead

epidermis, counteracting the stiffness of the toes and atrophy of the small muscles of the feet, reducing the hyperhidrosis, minimizing the pressure applied to the tender soles of the feet on walking, and decreasing the swelling.

If amputation was necessary, conservatism was practiced, and every effort was made to control infection. When large skin defects existed or when skin was lost on weight-bearing surfaces, various types of skin grafting were found to be helpful. Sympathectomy appeared to have a definite place in the treatment of only certain selected cases; in the majority of instances it was not indicated.

10. The purpose of the reconditioning program was to build up the general physical condition of the patient first and then to concentrate on the feet. The skin of the feet was hardened by such procedures as calisthenics in the pool and gymnasium, walking, and bicycling. At the same time, the small muscles of the feet were exercised in order to counteract the atrophy.

11. After the completion of the reconditioning program, 33 per cent of the series were returned to a limited type of duty. Most of the men in this group had a normal gait, were able to walk a mile or more, had no signs of hyperhidrosis, atrophy of muscles of the feet, or stiffness of the toes. Symptoms indicating nerve involvement were minimal, the mental outlook of the patients was satisfactory, and they did not have other medical or surgical defects.

Sixty-seven per cent of the series were discharged to civilian life. Most of the men in this group demonstrated signs of excessive sympathetic activity, walked poorly and only for short distances, complained of various types of paresthesias, or had lost portions of their toes and feet as a result of gangrene.

12. In conclusion, it is obvious from this study that trench foot is associated with a long period of at least partial physical incapacitation. The exact duration of this interval can only be determined by follow-up studies. In view of the fact that the sequelae of trench foot are aggravated by extremes of environmental temperatures, patients with this condition should, whenever possible, live in a place where a moderate climate exists most of the year.

The authors wish to express their appreciation to the many medical officers in overseas medical units, who first treated the patients in this series, and to the various ward officers at the Mayo General Hospital, and among them, particularly, Captains H. H. Lampert, R. H. Smith, P. B. Olsson, and R. Murray, who have helped generously in the study. They are also indebted to T/4 Adolph Schwartz and Cpl. Jacob W. Fite for their valuable assistance in the compilation of the data which form the basis for this report.

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THE CONSTRUCTION OF THE CARDIAC VECTOR

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A CERTAIN problem in connection with the construction of the cardiac vector representing the "manifest potential" has recently come to our attention.[1] Inasmuch as this problem may be a source of trouble and misunderstanding to other workers, and since it involves concepts which perhaps need further clarification, we shall discuss it in some detail.

The problem can be illustrated best by an example. Suppose the values of the potential at the right arm, left arm, and left leg are measured either by Wilson's common terminal technique[2] or by Goldberger's augmented-potential method,[3] and suppose we find that:

$$V_R = -3$$
$$V_L = +10$$
$$V_F = -7.$$

Then if we either measure the limb lead potential differences simultaneously or obtain them from the unipotential values, we would find, of course, that:

$$e_1 = +13$$
$$e_2 = -4$$
$$e_3 = -17.$$

Now let us construct the cardiac vector, using both sets of values, and let us call the construction using e_1, e_2, and e_3 Method I, and the construction using V_R, V_L, and V_F Method II.

Method I, following Bayley's notation,[4] is shown in Fig. 1. The three axes, representing the three limb lead directions, make angles of 60° with each other. Calling the cardiac vector E, we find that it has a magnitude of 17.8 units and makes an angle of 42° with the horizontal.

Method II makes use of the triaxial system formed by *OR*, *OL*, and *OF* in Einthoven's triangle (Fig. 2). *O* is the center of the triangle, at which the tail of the cardiac vector is located, and constitutes the origin of this second system. The new axes also make angles of 60° with each other, although they do not have the same directions as those of Method I. Actually, the second triaxial system consists of a rotation of the first through an angle of 30°. Using the

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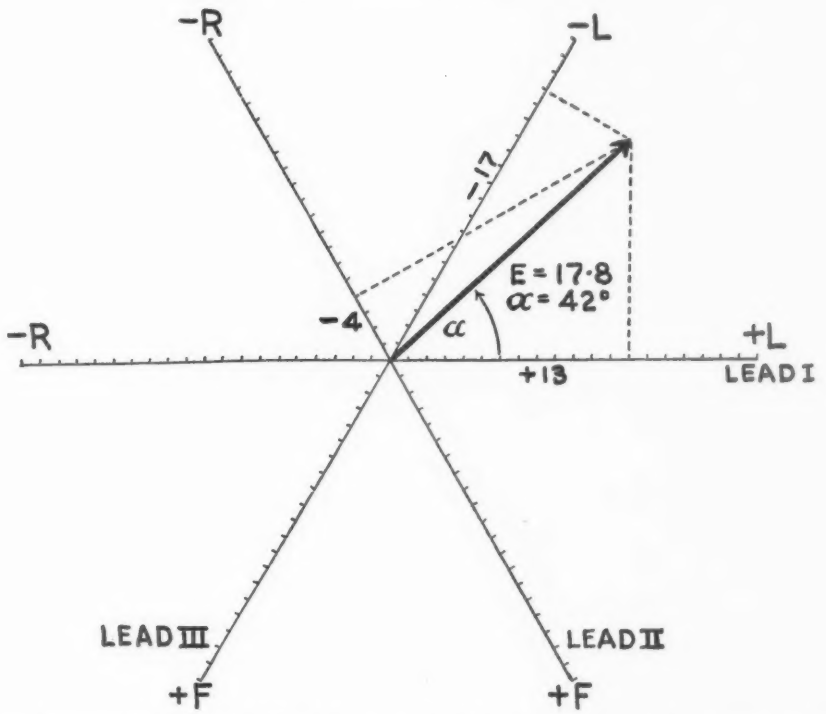

Fig. 1.—Construction of E by Method I. $e_1 = +13$, $e_2 = -4$, $e_3 = -17$. E is seen to be 17.8 units and $\alpha = 42°$.

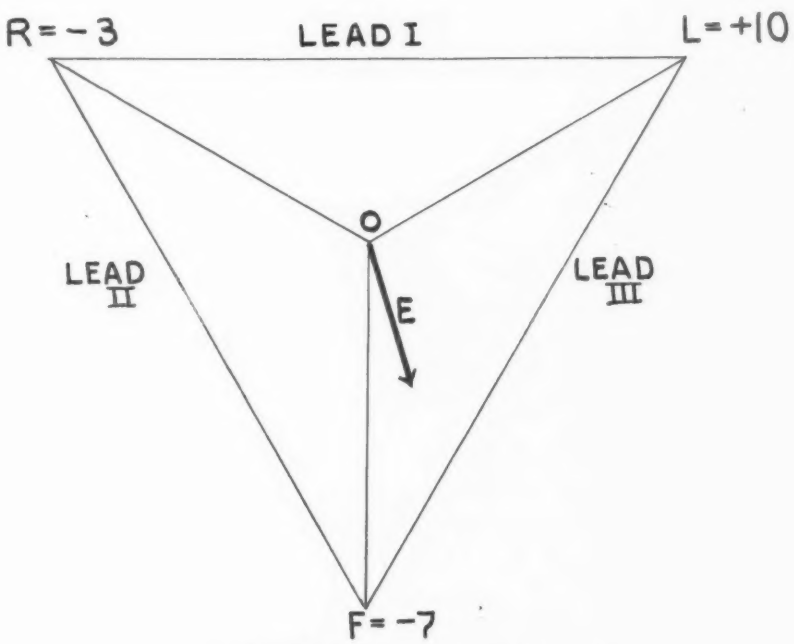

Fig. 2.—Einthoven's triangle.

values of V_R, V_L, and V_F given previously, we construct as in Method I. Fig. 3 shows the vector constructed by Method II. This time the resultant vector has a magnitude of 10.2 units, although it still makes an angle of 42° with the horizontal. Therefore, the result obtained by Method I is 17.8 units, which is $\sqrt{3}$ times higher than the result obtained by Method II, 10.2 units.

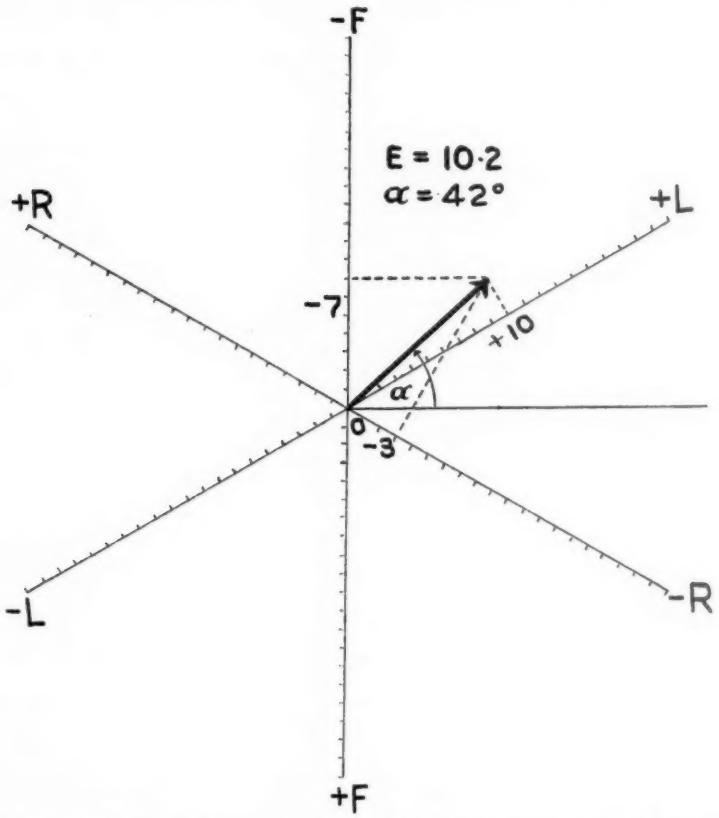

Fig. 3.—Construction of E by Method II. $V_R = -3$, $V_L = +10$, $V_F = -7$. E is now 10.2 units, while α is still 42°.

To illustrate further, let us suppose that we actually know in advance the magnitude and direction of E. To simplify the calculation, let E be 17.8 units and let it make an angle of 42° with the horizontal (Lead I). Then by reversing the procedure of Method I, we obtain

$$e_1 = +13$$
$$e_2 = -4$$
$$e_3 = -17.$$

The values of V_R, V_L, and V_F, obtained in a similar manner by reversing the procedure of Method II, are

$$V_L = +17.4$$
$$V_R = -5.3$$
$$V_F = -12.1.$$

This is shown in Fig. 4. From these values, we see that

$$e_1 = +22.7$$
$$e_2 = -6.8$$
$$e_3 = -29.5.$$

Evidently these values of e_1, e_2, and e_3 are $\sqrt{3}$ times higher than the values obtained by the direct projection of E on Leads I, II, and III, or, what amounts to the same thing, V_R, V_L, and V_F are $\sqrt{3}$ times higher than the originals.

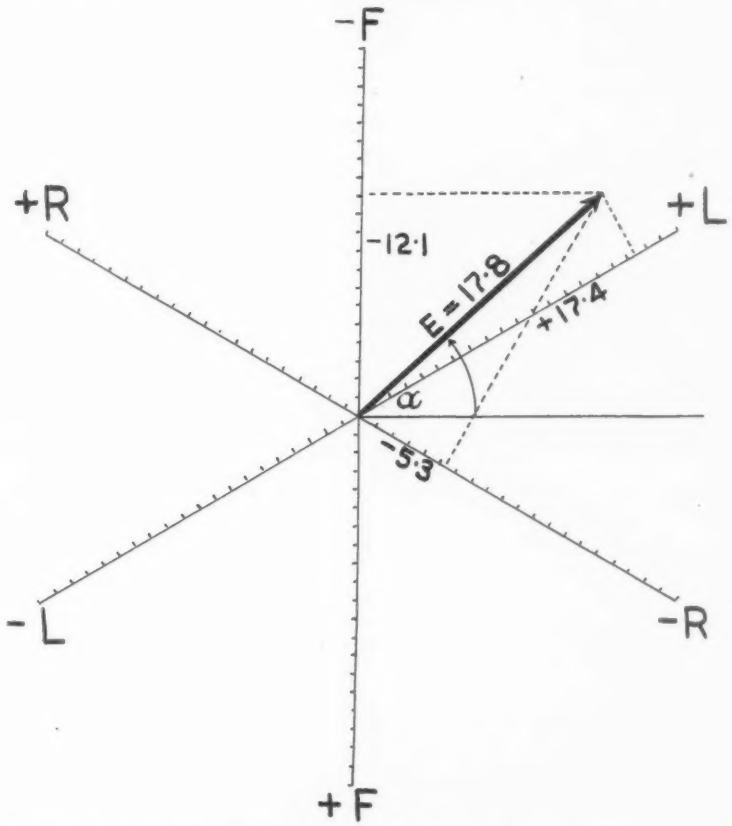

Fig. 4.—Resolution of E to find V_L, V_R, and V_F. E is assumed to be 17.8 units, and α is 42°. We find that $V_L = +17.4$, $V_R = -5.3$, $V_F = -12.1$.

To summarize: the cardiac vector as obtained by Method I is $\sqrt{3}$ times *higher* than the cardiac vector obtained by Method II. On the other hand, if we start with a given value of E, then the values of e_1, e_2 and e_3 obtained by direct projection onto the limb leads turn out to be $\sqrt{3}$ times *lower* than the values obtained by finding V_R, V_L, and V_F, followed by the necessary subtractions.

It is natural to ask which method is correct. The answer is "both." In order to explain this apparent discrepancy, we shall have to investigate the nature of what we are doing when we make these constructions. The present

paper is an attempt to clarify some misconceptions which appear to be fairly common.

Wilson and his co-workers,[5] Bayley,[6] and others have explained the nature of the cardiac vector and of the electric field which it produces. The reader is referred particularly to the section of Bayley's paper[6] which deals with vectors and electricity. For present purposes, we need only start with the concept that, at the heart, there exists an electrical force, which has at any instant a magnitude and direction and which can, therefore, be represented by a vector. Surrounding this vector is a field with a potential distribution, every point of which possesses a definite potential. By the potential of a point we mean the work which would be done if we brought a hypothetical unit positive charge from an infinite distance to the point in question. By the potential difference between any two points, we mean the work which would be done if we moved this charge from one point to the other. If we say that the potential or the potential difference is positive, we mean that we have had to do work and expend energy in this transit. If we say that it is negative, we mean that the electric field has done the work for us. Now work is not a vector quantity because there is no direction associated with it. Thus, in Fig. 5, the work done in going from *A*, which has a potential of +5, to *B*, which has a potential of +10, is +5 units, regardless of how we get from *A* to *B*. There are certain parts of Part II where the field will do the work for us and other parts where we will have to do the work; but the excess of what we do over what the field does, is always five units. Hence, it should be evident that neither the potential at a point such as V_R, V_L, or V_F nor the potential differences such as e_1, e_2, and e_3 involve a special direction, and that they are not, therefore, vectors.

It may be well to take up at this time another point, which explains why $e_2 = e_1 + e_3$, *a fact which has nothing whatever to do with Einthoven's triangle.* Instead of taking two points in the field, let us take any three points and let us give them any potentials we choose. Further, let us call them *R*, *L*, and *F*, oriented quite at random (Fig. 5, *b*). Let us go from *R* to *L* to *F* and back to *R*, calling the work done between *R* and *L*, e_1, between *L* and *F*, e_3, and between *F* and *R*, e_2 (in order to retain the electrocardiographic notation). e_1 is then –8, which means that in going from *R* to *L* the field helps us by doing 8 units of work; e_3 is +112, which means that in going from *L* to *F* we have to do 112 units of work; e_2 is –104, which means that in going from *F* to *R* the field does 104 units of work. The net amount of work done is –8 + 112 – 104, which is zero. This is a general fact, and it tells us that whenever we go around a closed loop, of any shape, and return to the starting point, the net amount of work done is zero. This is true for any number of stopping points above two, the only condition being that we get back to the starting point.

In the example above, we have seen that $e_1 + e_2 + e_3 = 0$. Now, if we arbitrarily reverse the sign of the work done between any two points, then obviously this work will equal the sum of all the other work done. That is exactly what is done in electrocardiography. The attachments to the galvanometer are

such that we measure the work done (potential difference) in going from F to R instead of from R to F. Therefore, e_2 is arbitrarily given a negative sign and we obtain

$$e_1 - e_2 + e_3 = 0 \quad \text{or}$$
$$e_1 + e_3 = e_2.$$

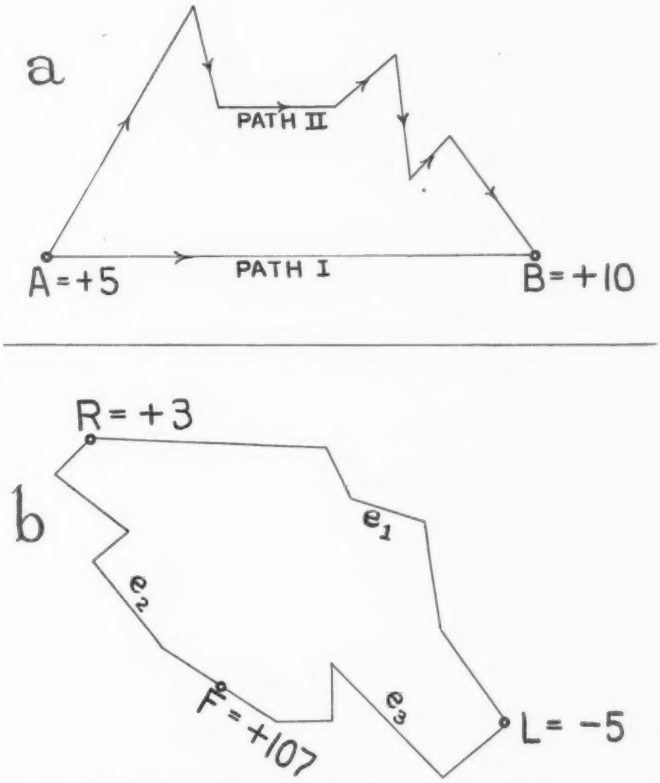

Fig. 5.—*a*, Two points in a scalar potential field. *b*, *R*, *L*, and *F* are any three points in a scalar potential field.

To return, then, to our original problem, in electrocardiography, *R*, *L*, and *F* are not oriented at random but are regarded as being located at the apices of an equilateral triangle. From what has been explained above, it is clear that none of the six quantities V_L, V_R, V_F, e_1, e_2, and e_3 has any necessary direction associated with it. These quantities are not vectors, but scalars, and, like all scalars, they can be added or subtracted in the same way that we can add two apples to eight apples or subtract two apples from eight apples. Therefore, it is possible to define e_1 as $V_L - V_R$, et cetera.

However, if we assign definite directions to these quantities, we can treat them as vectors. This is done, of course, by assigning to e_1, e_2, and e_3 the directions of the limb leads, i.e., the directions of the sides of the equilateral triangle; and by assigning to V_R, V_L, and V_F the directions *OR*, *OL*, and *OF*, respectively (Fig. 2). Now when these six quantities are transformed into vectors, they

must obey vector laws. They can no longer be simply added or subtracted. To illustrate what this means: if 1 is a scalar, then we can add 1 and 1 and obtain 2. If 1 is a vector, then the addition of two such vectors will give a resultant of 2 *only* when the two vectors are pointing in the same direction. If they make, for example, an angle of 90° with each other, then their sum is not 2 but $\sqrt{2}$. Hence it follows that, after becoming a vector, quantity e_1 is not necessarily equal to $V_L - V_F$. We have, in fact, given these six quantities six different directions.

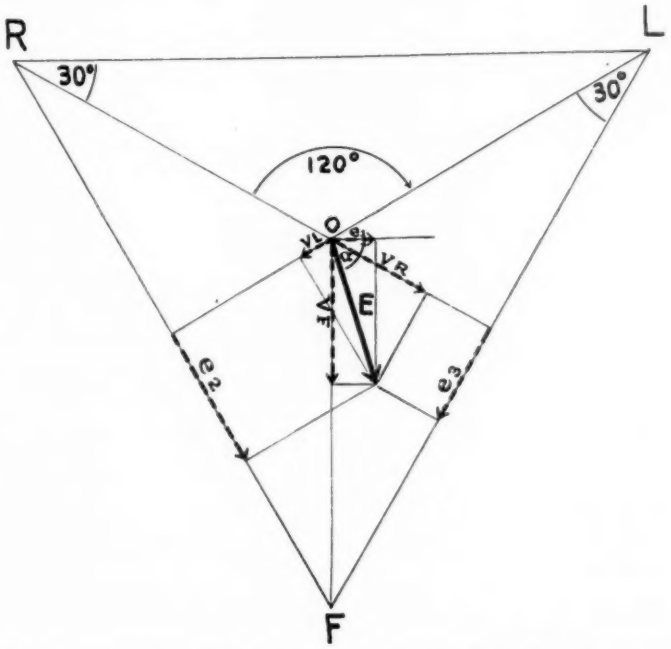

Fig. 6.—The six components of E are shown by broken lines, with arrowheads to denote that they are vectors. The magnitudes of the components can be expressed in terms of E and a. These magnitudes are given in the text.

The purpose in transforming these quantities into vectors is to enable us to treat these vectors as the projections or components of the cardiac vector E, which we call the "manifest potential difference" or the "electrical axis" of the heart. This is legitimate enough. Now, if e_1 is to be the projection of E in the direction of limb Lead I, then $V_L - V_F$, which has been defined as equal to e_1, should also be the projection of E in the direction of Lead I. But the definition of e_1 as $V_L - V_F$ was based on the essentially scalar nature of these quantities and does *not* carry over when they become vectors. This means that if, as in Fig. 1, $V_L = +10$ and $V_R = -3$, e_1 does *not* equal +13. Similarly, e_2 and e_3 must be dealt with as vectors and not as scalars. If Fig. 3, constructed for *vector* values of V_L, V_R, and V_F is correct, then Fig. 1 must have been constructed from the wrong *vector* values of e_1, e_2, and e_3 and must therefore be incorrect with respect to Fig. 3. On the other hand, if the vector values $e_1 = +13$, $e_2 = -4$, and $e_3 = -17$ are correct, thereby making Fig. 1 correct, then Fig. 2 is incorrect because we have used the wrong values for V_R, V_L, and V_F.

To find our way out of this difficulty, we only need find out how the component of E in the direction of Lead I *is* related to the difference between the components in the directions of *OL* and *OF*. In other words, how is vector e_1 related to the vector $(V_L - V_F)$? Vectors e_2 and e_3 must be similarly studied. As a matter of fact, these relationships already have been worked out, although not in the exact form in which they apply to this problem.[7] Fig. 6 should need no explanation. We must only keep in mind that all of the quantities used below are to be thought of as vectors. As usual, α is the angle between E and Lead I. Our six vectors are related to E and α by the following relationships:

$$\begin{aligned} e_1 &= E \cos \alpha \\ e_2 &= E \cos (\alpha - 60°) \\ e_3 &= E \cos (120° - \alpha) \\ V_R &= E \cos (210° - \alpha) \\ V_L &= E \cos (\alpha + 30°) \\ V_F &= E \sin \alpha \end{aligned}$$

The only other relationship we need is the familiar trigonometric one, $\cos (A \pm B) = \cos A \cos B \mp \sin A \sin B$.

Then

$$V_L - V_R = E \left[\cos (\alpha + 30°) - \cos (210° - \alpha) \right],$$

$$V_L - V_R = E \left[\frac{\sqrt{3}}{2} \cos \alpha - \frac{1}{2} \sin \alpha + \frac{1}{2} \sqrt{3} \cos \alpha + \frac{1}{2} \sin \alpha \right].$$

$$\therefore \; V_L - V_R = E \cos \alpha \cdot \sqrt{3} = e_1 \sqrt{3}.$$

Similarly

$$V_F - V_R = E \left[\sin \alpha - \cos (210° - \alpha) \right], \text{ and}$$

$$V_F - V_R = E \left[\frac{3}{2} \sin \alpha + \frac{1}{2} \sqrt{3} \cos \alpha \right].$$

But $e_2 = E \cos (\alpha - 60°) = E \left[\frac{1}{2} \cos \alpha + \frac{1}{2} \sqrt{3} \sin \alpha \right].$

Multiplying both sides by $\sqrt{3}$, we get

$$\sqrt{3}\, e_2 = E \left[\frac{\sqrt{3}}{2} \cos \alpha + \frac{3}{2} \sin \alpha \right].$$

$$\therefore \; V_F - V_R = e_2 \sqrt{3}.$$

Similarly

$$V_F - V_L = E \left[\sin \alpha - \cos (\alpha + 30°) \right], \text{ and}$$

$$V_F - V_L = E \left[\frac{3}{2} \sin \alpha - \frac{1}{2} \sqrt{3} \cos \alpha \right].$$

But $e_3 = \cos (120° - \alpha) = E \left[\frac{1}{2} \sqrt{3} \sin \alpha - \frac{1}{2} \cos \alpha \right].$

Multiplying both sides by $\sqrt{3}$, we get

$$\sqrt{3}\ e_3 = E\left[\frac{3}{2}\sin\alpha - \frac{1}{2}\sqrt{3}\cos\alpha\right].$$

$$\therefore\ V_F - V_L = e_3\sqrt{3}.$$

Summarizing,

$$V_L - V_R = e_1\sqrt{3}$$
$$V_F - V_R = e_2\sqrt{3}$$
$$V_F - V_L = e_3\sqrt{3}$$

The reason for the discrepancy between Figs. 1 and 3 is now obvious. Both constructions are perfectly valid but differ from each other by the proportionality constant $\sqrt{3}$. Therefore, two procedures are open to us: (a) We can use Method I, unchanged, on the limb lead potentials. However, if we then wish to use Method II on V_L, V_R, and V_F, we must make an adjustment either by multiplying V_L, V_R, and V_F each by $\sqrt{3}$ before constructing E, or by constructing E first and then multiplying its value by $\sqrt{3}$. (b) We can use Method II unchanged on V_R, V_L, and V_F. However, if we then wish to use Method I on e_1, e_2, and e_3, we must adjust either by dividing these values by $\sqrt{3}$ before constructing E, or by constructing E first and then dividing it by $\sqrt{3}$.

Since the equations defining these vector relationships contain no angles, either method, unaltered, will give the correct orientation of E.

As Wilson[8] and others have pointed out, the construction of the cardiac vector, E, is a very useful tool in clinical analysis, even though the vector so obtained does not give the actual magnitude* but only a quantity proportional to it. We have discussed in this paper another proportionality factor which must be taken into account when different methods of construction are used. To put the matter in simple comparative terms, it is as though Method I gives the value of E in feet, and Method II in yards, whereas E might really be expressible in miles. If we imagine that the relationship between the mile on the one hand, and feet and yards on the other, is unknown or unmeasured, then we will get a good picture of the actual significance of these constructions.

SUMMARY

1. Two methods of constructing the cardiac vector, E, differ from each other by a factor $\sqrt{3}$.

2. The quantities measured in electrocardiography are essentially scalar in nature; from this fact the independence of the relationship $e_1 + e_3 = e_2$, of Einthoven's triangle, follows.

3. The significance of a transformation of V_L, V_R, V_F, e_1, e_2, and e_3 into vectors was discussed. The relationship between these vectors was obtained and it was shown that both methods of construction are valid and equivalent and can be equalized, if one makes certain adjustments to account for the difference in orientation of the two triaxial reference systems.

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*The actual magnitude, as used here, refers to the magnitude of the projection of the spatial vector on the frontal plane. It was not necessary, in the above analysis, to discuss the three-dimensional cardiac vector.

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THE INCIDENCE OF PALPABLE DORSALIS PEDIS AND POSTERIOR TIBIAL PULSATIONS IN SOLDIERS

An Analysis of Over 1,000 Infantry Soldiers

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PALPATION for pulsations of peripheral arteries is an important clinical procedure. In the study of peripheral vascular diseases the presence or absence of a pulsation often gives a great deal of information. Pulsation may be absent in spasm, or as a result of organic changes in the palpated vessel. It is not sufficiently understood, however, that the absence of pulsation may also indicate a normal anatomic deviation. The radial artery pulsations are easily palpable and in normal individuals are rarely absent.

It has been a widely accepted opinion[3] that the dorsalis pedis and posterior tibial pulsations almost always can be palpated in normal individuals, or at least are very rarely absent. Buerger[1] studied 200 patients in whom the presence of peripheral vascular disease was carefully ruled out and found only in one instance an absence of the dorsalis pedis pulsation. This low incidence of absence of pulsations (0.5 per cent) compares favorably with the findings in a similar study of 381 patients by Erb.[2] In Erb's series an absence of both posterior tibial pulsations was noted in two patients, and an absent pulsation of the dorsalis pedis and posterior tibial of one foot was noted in two patients. An absent pulse was, therefore, observed in less than 1 per cent of those patients who presented no evidence of peripheral vascular disease.

This low incidence of absent pulsations in normal individuals has been challenged by other investigators. Morrison,[5] in an analysis of 1,000 individuals without symptoms of circulatory affections of the extremities, found an incidence of 19 per cent with absent pulsations of the dorsalis pedis and posterior tibial arteries. It should be mentioned that in Morrison's study two-thirds of the patients were women and that the ages varied widely. Reich[6] studied 500 healthy individuals and noted an absence of the dorsalis pedis pulsation in 4 per cent and an absence of the posterior tibial pulsation in 5 per cent of the patients. In an additional 8 per cent of the patients the dorsalis pedis pulsation was found in a position other than the usual one. In Schneyer's[7] analysis of 500 controls there was an absence of pulsation in 17 per cent of the men and 29 per cent of the women.

To supply further information on this problem the dorsalis pedis and posterior tibial pulsations were studied in 1,014 soldiers at an Army Infantry Training Center. Each soldier had completed his basic infantry training; the

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examination was part of the processing for overseas duty. As far as could be ascertained no soldier presented circulatory complaints of the lower extremities. The average age was 20 years; over 90 per cent of the soldiers examined were under 22 years of age. All the examinations were performed by the same medical officer. The subjects were divided into four groups, A, B, C, and D. Each group was examined at a different session, on a different day, but at a similar hour. Groups A, B, and C were composed of white men, and Group D was composed of Negroes. To insure accuracy Groups B and C were checked by another examiner. The pulsations were graded as "palpable" or "not palpable." Where a pulsation was weak, faint, or found at a slight distance from the usual location, it was considered palpable.

FINDINGS

A summary of the four groups examined is given in Table I. Of the 1,014 soldiers examined, 898, or 88.6 per cent, had a palpable right dorsalis pedis, and 116, or 11.4 per cent, had an absent right dorsalis pedis pulsation. In the

TABLE I. COMPOSITE TABLE OF PULSATIONS

GROUP	DORSALIS PEDIS RIGHT		POSTERIOR TIBIAL RIGHT		DORSALIS PEDIS LEFT		POSTERIOR TIBIAL LEFT	
	PALPABLE	NOT PALPABLE	PALPABLE	NOT PALPABLE	PALPABLE	NOT PALPABLE	PALPABLE	NOT PALPABLE
A (white)	330	47	370	7	326	51	373	4
377	87.5%	12.5%	98.1%	1.9%	86.3%	13.7%	98.9%	1.1%
B (white)	234	38	263	9	237	35	265	7
272	86.0%	14.0%	96.7%	3.3%	87.2%	12.8%	97.4%	2.6%
C (white)	230	29	255	4	213	46	252	7
259	88.8%	11.2%	98.5%	1.5%	82.2%	17.8%	97.3%	2.7%
D (Negro)	104	2	97	9	101	5	97	9
106	98.1%	1.9%	92.5%	7.5%	95.3%	4.7%	91.5%	8.5%
(A, B, C, D)	898	116	985	29	877	137	987	27
1,014	88.6%	11.4%	97.1%	2.9%	86.4%	13.6%	97.3%	2.7%

TABLE II. TABLE OF ABSENT PULSATIONS IN MORE THAN ONE ARTERY

GROUP	DORSALIS PEDIS AND POSTERIOR TIBIAL NOT PALPABLE RIGHT FOOT	DORSALIS PEDIS AND POSTERIOR TIBIAL NOT PALPABLE LEFT FOOT	DORSALIS PEDIS NOT PALPABLE BOTH FEET	POSTERIOR TIBIAL NOT PALPABLE BOTH FEET
A (white)	0	1	25	3
377	0.0%	0.3%	6.6%	0.8%
B (white)	2	1	28	3
272	0.7%	0.4%	10.3%	1.1%
C (white)	0	1	22	3
259	0.0%	0.4%	8.5%	1.2%
D (Negro)	0	0	1	8
106	0.0%	0.0%	0.9%	7.5%
(A, B, C, D)	2	3	76	17
1,014	0.2%	0.3%	7.5%	1.7%

left foot, 877 (86.4 per cent) had a palpable dorsalis pedis pulsation, and in 137 (13.6 per cent) this pulsation was absent. The posterior tibial pulsation on the right side was palpable in 985 (97.1 per cent) and absent in 29 (2.9 per cent). On the left side, the posterior tibial pulsation was palpable in 987 (97.3 per cent) and absent in 27 (2.7 per cent).

The number of absent pulsations in more than one artery is shown in Table II. Of the 1,014 soldiers examined, only two soldiers had an absent dorsalis pedis and an absent posterior tibial pulsation of the right foot, and in only three soldiers were these same pulsations absent in the left foot. There were 76 soldiers with an absent dorsalis pedis pulsation in both feet, an incidence of 7.5 per cent. In 17 soldiers there was an absence of both the posterior tibial pulsations in both feet, an incidence of 1.7 per cent.

TABLE III. TABLE OF COMPARISON OF PULSATIONS IN WHITE AND NEGRO SOLDIERS

	DORSALIS PEDIS RIGHT		POSTERIOR TIBIAL RIGHT		DORSALIS PEDIS LEFT		POSTERIOR TIBIAL LEFT	
RACE	PALPABLE	NOT PALPABLE	PALPABLE	NOT PALPABLE	PALPABLE	NOT PALPABLE	PALPABLE	NOT PALPABLE
White	794	114	888	20	776	132	890	18
(908)	87.4%	12.6%	97.8%	2.2%	85.6%	14.5%	98.0%	2.0%
Negro	104	2	97	9	101	5	97	9
(106)	98.1%	1.9%	92.5%	7.5%	95.3%	4.7%	91.5%	8.5%

The frequency of pulsations in the white and in the Negro soldier is shown in Table III. A significant difference was found in the two races. Whereas the right dorsalis pedis pulsation was absent in 12.6 per cent of the white men, this pulsation was absent in only 1.9 per cent of the Negroes. On the left side of the dorsalis pedis pulsation was absent in 14.5 per cent of the white men and in only 4.7 per cent of the Negroes. The situation was reversed when the posterior tibial pulsations were examined: approximately 2 per cent of the posterior tibial pulsations were absent in the white group and 8 per cent in the Negro group. When the absence of pulsation in more than one artery was studied (Table IV), the white soldiers showed a higher percentage of absence of both dorsalis pedis pulsations, whereas the Negro soldiers showed a higher percentage of absence of bilateral posterior tibial pulsations. Absence of both a dorsalis pedis and a posterior tibial pulsation in the same foot was very unusual. This occurred only five times in the 1,014 soldiers examined. In only one soldier of the entire series was the absence of pulsation of both the dorsalis pedis and posterior tibial in both feet observed.

TABLE IV. TABLE OF COMPARISON OF ABSENT PULSATIONS IN MORE THAN ONE ARTERY OF WHITE AND NEGRO SOLDIERS

RACE	DORSALIS PEDIS AND POSTERIOR TIBIAL NOT PALPABLE RIGHT FOOT	DORSALIS PEDIS AND POSTERIOR TIBIAL NOT PALPABLE LEFT FOOT	DORSALIS PEDIS NOT PALPABLE BOTH FEET	POSTERIOR TIBIAL NOT PALPABLE BOTH FEET
White	2	3	75	9
(908)	0.2%	0.3%	8.3%	1.0%
Negro	0	0	1	8
(106)	0.0%	0.0%	0.9%	7.5%

DISCUSSION

A clinical study of the incidence of pulsations is subject to certain criticisms. The interpretation of a pulsation is subjective, and its accuracy depends to a large extent upon the efficiency and experience of the examiner. Moreover, the environment in which the examination is performed will influence the results. A cold room, for example, may cause a barely palpable vessel to become impalpable. Emotional factors may influence the results, and in anxiety states the caliber of the blood vessels may be profoundly reduced. The physical condition of the patient at the time of the examination may affect the results. Such other conditions as a deformity of the foot, varicosities, edema, or obesity may make it difficult to palpate a normal vessel. Most studies dealing with this problem include women, thus introducing further variables. It is important to emphasize that this study was performed on a group of healthy, young soldiers chosen for the infantry.

The arterial blood supply of the foot is derived mainly from two arteries, the anterior tibial and the posterior tibial. The dorsalis pedis artery is really a continuation of the anterior tibial artery, extending downward to the proximal portion of the first intermetatarsal space. The posterior tibial artery is a continuation of the popliteal artery and extends downward to the groove between the internal malleolus and os calcis. It is these two arteries with their extensive series of anastomoses which insure a proper arterial supply to the foot. In man, however, this architectural arrangement is subject to many variations. As Reich[6] has pointed out, man differs from all other primates in this arterial distribution. In primates other than man, the blood supply of the foot comes directly from the femoral artery by way of a saphenous artery. This saphenous artery, not found in man, continues as the dorsalis pedis artery and gives off a posterior branch supplying the plantar aspect of the foot. This more direct arterial supply of the foot seen in other species of primates is therefore subject to less anatomic variation.

A normal variation of the arteries of the foot has been noted by anatomists. According to Gray[4] the dorsalis pedis artery may be larger than usual to compensate for a deficient plantar vessel, and "in 12 per cent of the bodies examined the dorsal pedis artery was so small as to be considered absent." Although no figures were given, Gray[4] noted that the posterior tibial artery was "not infrequently smaller than usual or absent." Clinically, therefore, one should normally expect to encounter absent dorsalis pedis and posterior tibial pulses in a small but definite percentage of cases. It was somewhat surprising, however, to find the incidence so high. Moreover, the incidence seemed to vary within the white and Negro races. This difference in frequency of pulses from a racial standpoint was commented upon by Reich,[6] who found, for example, that 4.9 per cent of the Japanese on whom observations had been made had an absent posterior tibial artery, as compared with 8.7 per cent of Europeans. In this study it was found that an absence of the dorsalis pedis pulse was decidedly more common in white persons than in Negroes. The reverse was true of the posterior

tibial pulsation. It was unusual to find an absent posterior tibial in white soldiers (2 per cent), whereas in the Negro soldier an absent posterior tibial pulse was more common (8 per cent). Regardless of race, when the dorsalis pedis pulsation was absent, a good posterior tibial was invariably found; and similarly when the posterior tibial pulsation was absent, a good dorsalis pedis was found. In only five instances (0.49 per cent) of the entire series of 1,014 subjects was this finding violated. This is understandable when one considers the architectural arrangement of the arteries of the foot. The collateral circulation of the foot is dependent upon an adequate anastomosis of the posterior tibial and dorsalis pedis arteries. It is apparent, then, that a reduction in the size of the dorsalis pedis artery, for example, will be accompanied by a corresponding increase in the size of the posterior tibial artery. From a practical standpoint it is well to remember that in normal individuals an absence of both the dorsalis pedis and posterior tibial pulsations on the same side is anatomically unsound and decidedly uncommon. An absent dorsalis pedis and posterior tibial pulse on the same side would, therefore, seem to have more clinical significance than an absence of bilateral dorsalis pedis or an absence of bilateral posterior tibial pulsations. The order of importance to be attached to normal absence of pulsation in soldiers of the two races is shown in Table V.

TABLE V. PULSATIONS OF FOOT ARRANGED ACCORDING TO ORDER OF ABSENCE

WHITE	NEGRO
1. Left dorsalis pedis (14.5%)	1. Left posterior tibial (8.5%)
2. Right dorsalis pedis (12.6%)	2. Right posterior tibial (7.5%)
3. Right and left dorsalis pedis (8.3%)	3. Right and left posterior tibial (7.5%)
4. Right posterior tibial (2.2%)	4. Left dorsalis pedis (4.7%)
5. Left posterior tibial (2%)	5. Right dorsalis pedis (1.9%)
6. Right and left posterior tibial (1%)	6. Right and left dorsalis pedis (0.9%)
7. Left dorsalis pedis and left posterior tibial (0.3%)	7. Right dorsalis pedis and right posterior tibial (0%)
8. Right dorsalis pedis and right posterior tibial (0.2%)	8. Left dorsalis pedis and left posterior tibial (0%)

SUMMARY

1. The incidence of palpable dorsalis pedis and posterior tibial pulsations was studied in 1,014 infantry soldiers; in over 13 per cent one or more pulses was absent.

2. The incidence of palpable pulsations in these arteries was different in white and Negro soldiers. The posterior tibial pulse was more frequently absent in the Negro, and the dorsalis pedis pulse was more frequently absent in the white soldier.

3. Absence of both the dorsalis pedis and the posterior tibial pulses on the same side was most unusual. This combination occurred in only five instances of the entire series.

4. The posterior tibial and dorsalis pedis arteries in man are subject to wide anatomic variations. In interpreting an absent pulsation in the foot one should be aware of these normal variations.

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THE RATES OF WATER AND HEAT LOSS FROM THE RESPIRATORY TRACT OF PATIENTS WITH CONGESTIVE HEART FAILURE WHO WERE FROM A SUBTROPICAL CLIMATE AND RESTING IN A COMFORTABLE ATMOSPHERE

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BECAUSE of the importance of the disturbances in water balance in congestive heart failure, any knowledge of the nature of water loss from the respiratory tract is significant. The dyspnea and accumulation of water in the lungs in congestive heart failure makes a study of this sort even more interesting. As shown previously,[1] the rate of heat and water loss is influenced by the conditions of the environment, particularly hot and humid environments. The latter type of environment was found to disturb the patient in congestive heart failure a great deal[2] thus further increasing the need of a study of water and heat loss from the respiratory tract in heart failure. Such observations are wanting, for a review of the literature revealed only one paper[3] concerned with such studies. With these facts in mind, a study was undertaken to investigate quantitatively the rates of water and heat loss from the respiratory tract of patients with congestive heart failure who rested sitting in a comfortable atmosphere.

METHODS AND MATERIALS

The methods employed for the measurement of water and heat loss were described previously.[4] Space does not permit a repetition of the description of the methods in detail in this report. In brief, the water loss was measured by having the subjects exhale through aluminum coils cooled by carbon dioxide snow. By means of suitable valves and gas meters the subjects would inspire room air and expire the water laden air through the collecting coils where the water was condensed. Simultaneously, the water content of an equal volume of room air was measured by the same method. The volume of air irrigating the respiratory tract per unit of time was recorded by the gas meters. By weighing the aluminum coils on an analytical balance before and after the collecting of the water and simultaneously measuring the water content of the air inspired, the rate of water loss from the respiratory tract became known.

To measure the heat loss simultaneously with the measurement of water loss from the respiratory tract, thermocouples were inserted in the afferent and efferent paths of the respired air. This made it possible to learn the heat exchange by warming or cooling inspired air. From the water loss, heat loss from evaporation was calculated. From the volume of carbon dioxide liberated, the heat loss from the decomposition of carbonic acid was learned. The total rate of

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heat loss from the body was measured by the ordinary clinical type of basal metabolism apparatus. From these methods (see previous report[4] for details) it was possible to measure quantitatively: (1) the rate of respiration, (2) the volume of tidal air, (3) the rate of irrigation of the respiratory tract with air, (4) the rate of carbon dioxide liberation, (5) the rate of heat loss from carbon dioxide liberation, (6) the rate of water loss, (7) the rate of heat loss from the evaporation of water, (8) the temperature of the expired air, (9) the relative humidity of the expired air, (10) the heat loss or gain by the warming or cooling of inspired air, (11) the relationships of each component of heat loss from the respiratory tract to the total heat loss, and (12) the relationship of heat loss from the respiratory tract to total body heat loss.

The 24 subjects employed in these studies suffered from uncomplicated right and left congestive heart failure. The etiology of the failure varied; hypertension, arteriosclerosis, syphilis, rheumatic fever, or "toxic" myocarditis (precise nature unknown) was the cause in descending order of frequency. The age, sex, and color distributions are indicated by Tables I and II. All of the patients were in Functional Class IV[5] during the studies, except for Subjects 1 and 2, whose state of cardiac function varied while under repeated observations for several weeks. Although all of the patients were bedridden because of their heart failure, none of them were in a state of peripheral circulatory collapse and none were moribund. All of them had marked dyspnea, orthopnea, fine moist râles in the bases of the lungs, edema of the feet and legs, a large liver, and the other usual symptoms and signs of congestive heart failure. With only two exceptions the patients showed either beginning cardiac compensation or no change in the functional capacity of the heart. In the two subjects the state of the heart failure was progressively becoming worse during hospitalization and study. All patients were receiving treatment for congestive heart failure. This included bed rest, low salt intake, digitalis, and diuretics, including intravenous mercurial diuretics. Two subjects had auricular fibrillation.

The subjects were transported from Charity Hospital to the laboratory at Tulane. They rested in the sitting position during the entire study, resting for at least thirty minutes before any observations were begun. It required approximately thirty minutes to complete the observations. The conditions of the environment are indicated by Tables I and II. Repeated measurements were made on some of the subjects. All patients were dressed in a cotton hospital type of gown and then covered from the waist down with a cotton sheet.

During the course of the study of these patients, patients with other disease states and normal subjects were observed as controls. The results on the normal subjects were reported previously.[1] Data from the paper will be employed freely for purposes of comparison. The studies on the patients with other disease states will be reported in detail as a group at a later date.

RESULTS

The results are summarized by Tables I and II and Figs. 1 and 2.

The Rate of Water Loss.—In a comfortable environment with a mean temperature of 20.1° C. (extremes, 19.5° and 21.1°) and a mean relative humid-

ity of 56 per cent (extremes, 47 and 67),* the mean rate of water loss for the 24 patients with congestive heart failure was 0.944 Gm. per square meter of surface area per ten minutes, the extremes being 0.625 and 1.482 (Table I). When the room conditions were changed slightly by raising the temperature 1.4° C. (mean, 21.5° C.; extremes, 21.1° and 22.2°) and lowering the relative

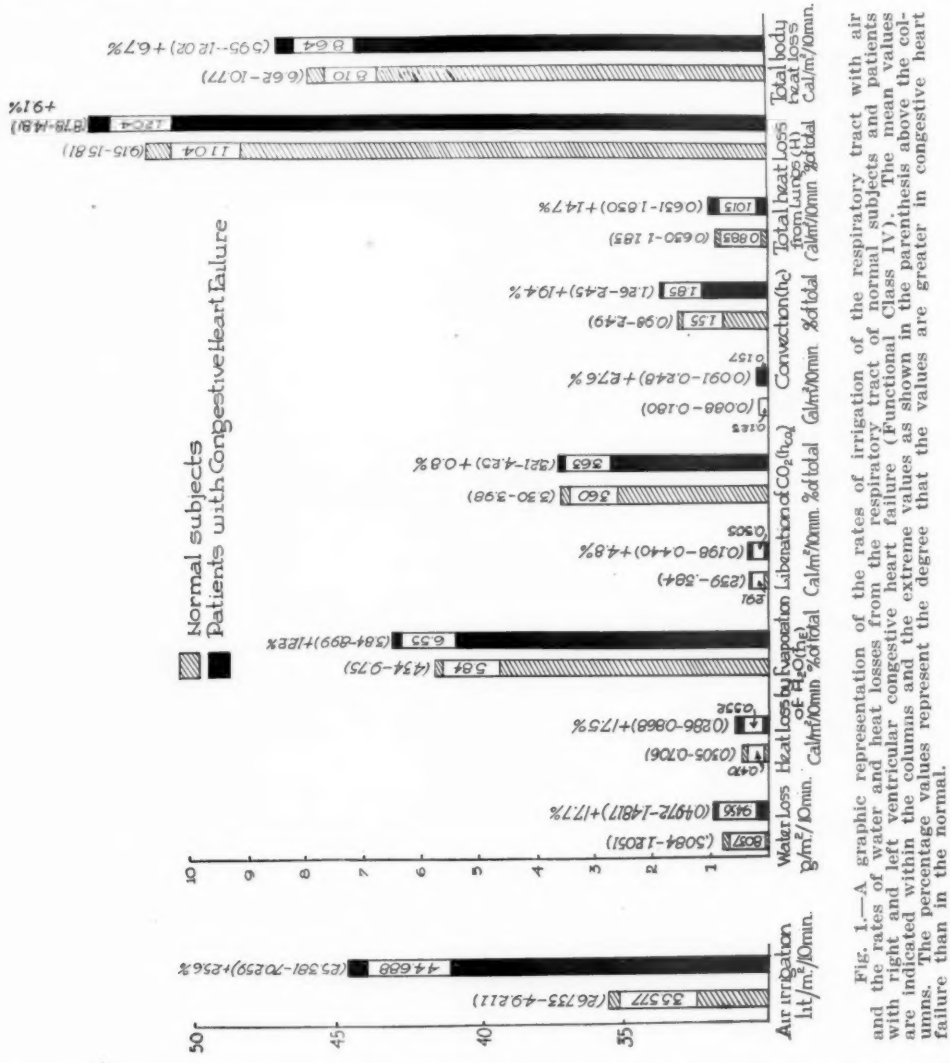

Fig. 1.—A graphic representation of the rates of irrigation of the respiratory tract with air and the rates of water and heat losses from the respiratory tract of normal subjects and patients with right and left ventricular congestive heart failure (Functional Class IV). The mean values are indicated within the columns and the extreme values as shown in the parenthesis above the columns. The percentage values represent the degree that the values are greater in congestive heart failure than in the normal.

humidity somewhat (mean, 51 per cent, extremes, 43 and 57),* the rate of water loss remained essentially unchanged (mean, 1.052; extremes, 0.694 and 1.456 Gm. per square meter of surface area per ten minutes). Under both environmental conditions the room atmosphere was comfortable. The statistical constants are shown in Tables I and II.

*This will be known as the comfortable environment at 20° C. and the comfortable environment at 21.5° C.

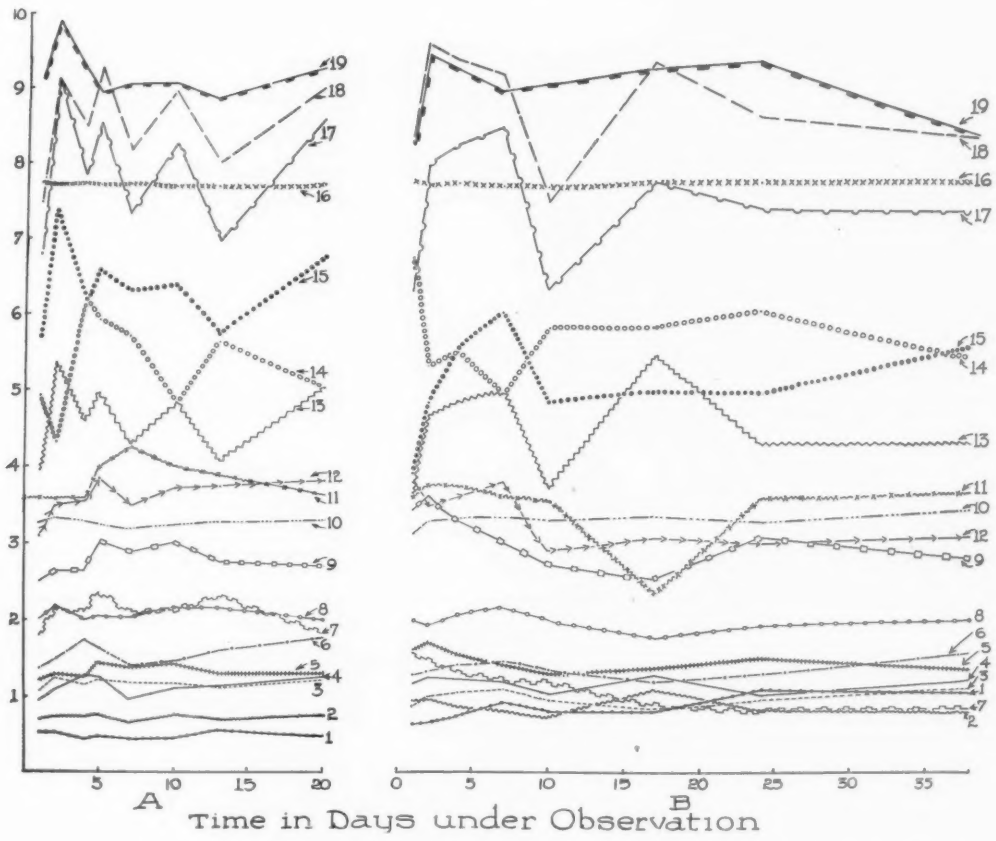

Fig. 2.—The results of repeated measurements upon two patients with congestive heart failure studied over a period of three or more weeks. *A* shows the results upon Patient 1 and *B* on Patient 2. The various lines shown represent the measurements and units indicated. In order to use a common ordinate the true value, V, was reduced or increased by multiples of ten as indicated. *1* = respiratory volume in c.c. $\frac{V}{(1000)}$. *2* = Rate of total body heat loss in calorie per square meter of surface area per ten minutes $\frac{(V)}{10}$. *3* = Rate of total loss of heat from the respiratory tract. H. in calorie/M.² surface area/ten minutes (V × 10). *4* = Rate of heat loss by convection, h_c, from the respiratory tract in calorie/M.²/ten minutes (V × 10). *5* = Rate of carbon dioxide loss in liters/M.²/ten minutes (V). *6* = Rate of heat loss by convection, h_c, as percentage of total body heat loss (V × 10). *7* = Rate of respiration in minutes $\frac{(V)}{10}$. *8* = Dry bulb temperature of environment in ° C. $\frac{(V)}{10}$. *9* = Rate of heat loss from carbon dioxide excretion, h_{CO_2}, in calorie/M.²/ten minutes (V × 10). *10* = Temperature of the expired air in ° C. $\frac{(V)}{10}$. *11* = Rate of heat loss from the excretion of carbon dioxide as percentage of total body heat loss in calorie/M.²/ten minutes (V). *12* = Rate of irrigation of the respiratory tract with air in liters/M.²/ten minutes $\frac{(V)}{10}$. *13* = Rate of heat loss by the vaporization of water, h_e, in calorie/M.²/ten minutes (V × 10). *14* = Relative humidity of the room air in percentage $\frac{(V)}{10}$. *15* = Rate of heat loss by the vaporization of water as percentage of total body heat loss in calorie/M.²/ten minutes (V). *16* = Barometric pressure of room atmosphere in mm. Hg $\frac{(V)}{100}$. *17* = Rate of water loss in grams/M.²/ten minutes (V × 10). *18* = Rate of total heat loss from the respiratory tract in calorie/M.²/ten minutes (V × 10). *19* = Relative humidity of the expired air in percentage $\frac{(V)}{10}$.

TABLE I. THE CONDITIONS OF THE ROOM ATMOSPHERE AND THE RATES OF WATER AND HEAT LOSSES FROM THE RESPIRATORY TRACT OF TWENTY-ONE PATIENTS WITH FUNCTIONAL CLASS IV RIGHT AND LEFT VENTRICULAR CONGESTIVE HEART FAILURE. THE PATIENTS RESTED SITTING QUIETLY IN A COMFORTABLE ROOM AT 20.1° C.

											RATE OF HEAT LOSS								
				ENVIRONMENT		AIR IRRIGATING LUNGS	CO_2 EXHALED	EXPIRED AIR		WATER LOSS	VAPORIZED WATER		LIBERATION OF CO_2		WARMING AIR		TOTAL LOSS FROM LUNGS		TOTAL BODY HEAT LOSS
SUBJECT	AGE YR.	SEX	RACE	D. B.† °C.	R.H.‡ %	l./M.²/10*	l./M.²/10*	D. B.† °C.	R.H.‡ %	GM./M.²/10*	CAL./M.²/10*	% TOTAL	CAL./M.²/10*	% TOTAL	CAL./M.²/10*	% TOTAL	CAL./M.²/10*	% TOTAL	CAL./M.²/10*
1	44	F	N	20.1	49	31.202	1.200	31.2	91	0.6766	0.396	5.66	0.252	3.60	0.096	1.37	0.744	10.65	7.00
				19.9	62	35.601	1.259	33.1	92	0.7755	0.454	6.17	0.264	3.59	0.127	1.73	0.845	11.48	7.36
				20.6	59	38.350	1.444	32.7	89	0.8492	0.498	6.55	0.303	3.99	0.125	1.64	0.926	12.18	7.60
				20.3	57	35.189	1.375	32.0	90	0.7307	0.428	6.29	0.289	4.25	0.095	1.40	0.812	11.94	6.80
				20.0	50	38.171	1.288	33.1	92	0.8543	0.501	6.74	0.270	3.63	0.125	1.68	0.896	12.06	7.43
2	38	F	N	20.0	67	38.002	1.616	31.1	82	0.6252	0.366	3.91	0.339	3.63	0.118	1.26	0.823	8.80	9.35
				19.5	53	34.667	1.727	32.8	94	0.7925	0.464	4.80	0.363	3.76	0.125	1.29	0.952	9.86	9.66
				20.9	55	36.123	1.557	33.4	92	0.8220	0.482	5.53	0.327	3.75	0.122	1.40	0.931	10.68	8.72
				20.0	58	28.713	1.293	33.1	90	0.6273	0.368	4.82	0.272	3.56	0.102	1.34	0.742	9.72	7.63
				19.5	60	30.307	1.486	33.1	93	0.7336	0.430	4.93	0.312	3.58	0.113	1.30	0.855	9.81	8.72
				20.0	54	30.962	1.357	34.2	84	0.7344	0.430	5.52	0.285	3.66	0.120	1.54	0.835	10.72	7.79
3	41	F	N	20.0	47	63.796	1.583	31.7	94	1.4157	0.830	8.99	0.332	3.60	0.205	2.22	1.367	14.81	9.23
				19.5	47	53.479	1.376	32.2	87	1.0912	0.639	7.86	0.289	3.55	0.186	2.29	1.114	13.70	8.13
4	54	F	N	20.6	67	49.412	1.211	32.5	84	0.9073	0.532	6.96	0.254	3.32	0.161	2.11	0.947	12.40	7.64
5	34	F	W	20.9	53	51.436	1.440	33.1	90	1.0640	0.624	7.54	0.302	3.65	0.172	2.08	1.098	13.26	8.28
6	52	F	N	20.0	62	56.001	1.461	33.5	90	1.1830	0.693	8.20	0.307	3.63	0.207	2.45	1.207	14.28	8.45
7	17	F	N	20.6	59	41.187	0.944	32.2	87	0.8484	0.497	8.35	0.198	3.33	0.131	2.20	0.826	13.88	5.95
8	18	F	N	20.0	60	44.172	1.649	33.9	92	1.1582	0.679	6.93	0.346	3.53	0.169	1.72	1.194	12.18	9.80
9	68	M	W	20.0	50	50.212	1.689	32.8	89	1.0672	0.625	6.65	0.355	3.78	0.176	1.87	1.156	12.30	9.40
10	27	F	N	20.0	59	32.946	1.305	33.6	83	0.7410	0.434	5.75	0.274	3.63	0.122	1.62	1.830	10.99	7.55
11	54	M	N	20.3	51	58.000	1.478	32.2	83	1.1430	0.667	7.60	0.310	3.53	0.189	2.15	1.116	13.28	8.78
12	54	M	N	20.3	57	63.055	2.096	33.4	83	1.1276	0.661	5.50	0.440	3.66	0.226	1.88	1.327	11.04	12.02
				20.0	55	70.259	1.844	32.9	87	1.4817	0.868	8.27	0.387	3.69	0.248	2.36	1.503	14.31	10.50

*All units are in M.² per ten minutes.
†D. B. = Dry bulb.
‡R. H. = Relative humidity.

13	67	M	N	20.0	54	55.908	1.464	33.1	82	1.2063	0.707	8.29	0.307	3.60	0.200	2.34	1.214	14.23	8.53
14	52	M	N	20.3	56	44.204	1.442	33.6	91	1.0940	0.641	7.60	0.303	3.59	0.161	1.91	1.105	13.11	8.43
15	27	F	N	20.0	67	48.909	1.437	34.1	96	1.2034	0.692	8.41	0.302	3.67	0.188	2.28	1.182	14.36	8.23
16	44	F	W	20.3	63	44.232	1.446	33.7	79	0.8000	0.460	5.41	0.304	3.58	0.182	1.91	0.926	10.89	8.50
				19.7	57	47.897	1.446	33.6	86	0.8773	0.504	6.09	0.304	3.67	0.182	2.20	0.990	11.96	8.28
17	53	F	N	20.5	57	25.381	1.075	33.6	83	0.5421	0.312	4.76	0.228	3.48	0.091	1.39	0.631	9.62	6.56
				20.3	57	26.350	1.294	33.6	77	0.4972	0.286	3.84	0.272	3.65	0.096	1.29	0.654	8.78	7.45
18	49	M	W	19.7	59	53.972	1.579	33.9	74	0.9638	0.554	5.89	0.332	3.53	0.201	2.23	1.096	11.66	9.40
19	35	M	N	20.0	57	35.619	1.256	33.6	81	0.6801	0.391	5.37	0.264	3.63	0.132	1.81	0.787	10.81	7.28
Statistical constants						44.9285±	1.4471±	33.09±	87.6±	0.94429±	0.5525±	6.536±	0.3006±	3.632±	0.1597±	1.861±	1.0500±	12.050±	8.422±
Mean						1.8263	0.5627	2.09	1.5	0.05809	0.0334	0.174	0.0116	0.031	0.0084	0.078	0.0496	0.397	0.309
Range				19.5	47	25.381	0.944	31.1	74	0.4972	0.286	3.84	0.198	3.32	0.091	1.26	0.631	8.78	5.95
				21.1	67	70.259	2.096	34.2	96	1.4817	0.868	8.99	0.440	4.25	0.248	2.45	1.830	14.81	12.02
Standard deviation						16.020±	0.4936±	1.8±	13±	0.5096±	0.293±	1.53±	0.102±	0.27±	0.074±	0.68±	0.435±	3.48±	2.71±
						1.291	0.040	1.5	1	0.0411	0.024	0.12	0.008	0.02	0.006	0.06	0.035	0.28	0.22
Coefficient of variation						35.6±	3.41±	5.5±	14.8±	53.9±	53.0±	23.4±	33.93±	7.46±	46.34±	36.54±	41.4±	28.88±	32.18±
						3.2%	0.28%	0.6%	0.1%	5.5%	0.4%	1.9%	3.03%	0.61%	4.47%	3.320%	3.8%	2.52%	2.9%

TABLE II. THE CONDITIONS OF THE ROOM ATMOSPHERE AND THE RATES OF WATER AND HEAT LOSSES FROM THE RESPIRATORY TRACT OF PATIENTS WITH FUNCTIONAL CLASS IV RIGHT AND LEFT VENTRICULAR CONGESTIVE HEART FAILURE. THE PATIENTS RESTED SITTING QUIETLY IN A COMFORTABLE ROOM AT 21.5° C.

												RATE OF HEAT LOSS								
				ENVIRONMENT		AIR IRRIGATING LUNGS	CO_2 EXHALED	EXPIRED AIR		WATER LOSS	VAPORIZED WATER		LIBERATION OF CO_2		WARMING AIR		TOTAL LOSS FROM LUNGS		TOTAL BODY HEAT LOSS
SUBJECT	AGE YRS.	SEX	RACE	D. B.† ° C.	R.H.‡ %	L./M.²/ 10*	L./M²/ 10*	D. B.† ° C.	R. H.‡ %	GM./M.² /10*	CAL./ M.²/ 10*	% TOTAL	CAL./ M.²/ 10*	% TOTAL	CAL./ M.²/ 10*	% TOTAL	CAL./ M²/ 10*	% TOTAL	CAL./ M.²/ 10*
1	44	F	N	21.8	43	34.886	1.259	33.3	99	0.9107	0.534	7.26	0.264	3.59	0.108	1.47	0.906	12.32	7.36
	44	F	N	21.7	48	37.266	1.444	32.5	90	0.8219	0.482	6.34	0.303	3.99	0.110	1.45	0.895	11.78	7.60
				21.7	56	37.388	1.310	32.8	88	0.6938	0.407	5.72	0.275	3.86	0.114	1.60	0.796	11.18	7.12
2	38	F	N	21.7	49	37.975	1.422	33.4	89	0.8438	0.494	5.99	0.299	3.62	0.120	1.45	0.913	11.07	8.25
22	35	M	N	21.1	56	57.469	1.488	33.6	83	1.0737	0.629	7.31	0.312	3.63	0.196	2.28	1.137	13.22	8.60
				21.1	44	57.178	1.769	33.4	89	1.3322	0.781	7.63	0.371	3.63	0.192	1.88	1.344	13.14	10.23
				21.1	56	58.305	1.769	32.8	90	1.2978	0.760	7.43	0.371	3.63	0.186	1.82	1.317	12.87	10.23
				21.1	56	51.304	1.320	32.5	93	1.1506	0.674	8.73	0.277	3.59	0.160	2.07	1.111	14.39	7.72
23	64	M	W	21.4	51	42.070	1.515	33.4	85	0.8569	0.502	5.55	0.318	3.51	0.137	1.51	0.959	10.60	9.05
24	31	M	N	22.0	52	47.146	1.662	34.8	83	1.0740	0.629	6.74	0.349	3.74	0.165	1.77	1.143	12.25	9.33
4	54	F	N	21.1	44	50.175	1.454	33.4	85	1.1139	0.652	7.70	0.305	3.60	0.169	2.00	1.126	13.29	8.49
10	59	M	N	22.2	57	74.238	1.996	33.6	83	1.4560	0.853	7.39	0.419	3.63	0.231	2.00	1.503	13.02	11.54
14	52	F	N	21.1	56	42.317	1.383	34.2	87	1.0548	0.618	7.67	0.290	3.60	0.152	1.89	1.060	13.15	8.06
Mean				21.5	51	48.286	1.522	33.4	88	1.0523	0.617	7.04	0.319	3.66	0.157	1.78	1.093	12.48	8.74
Range				21.1	43	37.266	1.259	32.5	83	0.6938	0.407	5.55	0.264	3.51	0.108	1:45	0.796	10.60	7.12
				22.2	57	74.238	1.996	34.8	99	1.4560	0.853	8.73	0.419	3.99	0.231	2.28	1.503	14.39	11.54
Standard deviation						11.447± 2.245	0.203± 0.040	0.65± 0.13	4.6± 0.9	0.217± 0.043	0.126± 0.025	0.921± 0.181	0.044± 0.009	0.13± 0.03	0.031± 0.006	0.26± 0.05	0.208± 0.041	1.041± 0.204	1.15± 0.23
Coefficient of variation						23.70± 4.65%	13.34± 2.62%	1.94± 0.38%	5.19± 1.02%	20.62± 4.04%	20.42± 4.00%	13.08± 2.57%	13.79± 2.70%	3.52± 0.69%	1.94± 0.38%	14.38± 2.82%	19.03± 3.73%	8.34± 1.64%	13.16± 2.58%

*All units are in M.² per ten minutes.
†D. B. = Dry bulb.
‡R. H. = Relative humidity.

Temperature of the Expired Air.—The mean temperature of the expired air was 33.1° C. (extremes, 31.1 and 34.2) for the comfortable environment at 20° C. When the environment was changed to 21.5° C., the mean temperature of the expired air was 33.4° C. (extremes, 32.5 and 34.8). The statistical constants are shown in Tables I and II.

Relative Humidity of the Expired Air.—The mean relative humidity of the expired air was 87 per cent (extremes, 82 and 94) when the patients were in the room at 20° C. When the temperature of the room was changed to 21.5° C. the mean value increased to 88 per cent (extremes, 83 and 96). The value of 96 per cent (Table I) is most probably an erroneous value. This was the only such value obtained under the above room conditions. The statistical constants are found in Tables I and II.

Rate of Irrigation of the Respiratory Tract With Air.—In the comfortable environment at 20° C., the mean rate at which the respiratory tract was irrigated with air was 44.929 liters per square meter of body surface area per ten minutes (extremes, 25.381 and 70.259). In the room atmosphere at 21.5° C. the mean rate was 48.286 liters per square meter of body surface area per ten minutes (extremes, 37.266 and 74.238). The statistical constants are indicated by Tables I and II.

There was a high positive correlation between the rate of water loss and the rate of irrigation of the respiratory tract with air, the coefficient of correlation being 0.9346 ± 0.0144. The coefficient of correlation between the rate of irrigation of the respiratory tract to the rate of total body heat production (oxygen consumption) was 0.6449 ± 0.0666.

Rate of Heat Loss From the Respiratory Tract.—The mean rate of heat loss by the vaporization of water, h_e, 0.553 calorie per square meter of body area per ten minutes (extremes, 0.286 and 0.868) when the comfortable environment was at 20° C. and 0.617 (extremes, 0.407 and 0.853) when the environment was at 21.5° C. This represented an average of 6.55 per cent (extremes, 3.84 and 8.99) of the total heat lost from the body and about 54.5 per cent (extremes, 28.2 and 85.7) of the total heat lost from the respiratory tract.

The mean rate of heat loss by convection or warming inspired air, h_c, was 0.157 calorie per square meter of body area per ten minutes (extremes, 0.108 and 0.231) at the 21.5° C. environment. This represented a mean of about 1.85 per cent (extremes, 1.26 and 2.45) of the total heat lost from the body and about 15.5 per cent (extremes, 9 and 24.5) of the total lost from the respiratory tract.

The mean rate of heat loss by the decomposition of carbonic acid with the expiration of carbon dioxide, h_{CO_2} was 0.305 calorie per square meter of surface area per ten minutes (extremes, 0.198 and 0.440) for the comfortable temperature at 20° C. The mean rate was 0.319 calorie per square meter of body surface per ten minutes (extremes, 0.264 and 0.419) for the room temperature of 21° C. The heat lost from the expiration of carbon dioxide represented about 3.63 per cent (extremes, 3.32 and 4.25) of the total loss of body heat or 30.1 per cent (extremes, 19.6 and 43.4) of the total heat lost from the respiratory tract.

The mean rate of total loss of heat from the respiratory tract was 1.013 calories per square meter of body area per ten minutes (extremes, 0.631 and 1.830) when the comfortable room temperature was 20° C. and a mean of 1.093 (range, 0.796 to 14.81) of the total heat lost from the body.

The mean rate of total heat loss from the body was 8.20 calories per square meter of body surface area per ten minutes (extremes, 6.56 and 10.50) when the subjects rested in a comfortable environment at 20° C.; the mean rate was 8.74 (extremes, 7.12 and 11.54) at a room temperature of 21° C.

Individual variations for each component of heat loss are given in detail in Tables I and II.

Prolonged Period of Study in Two Patients.—Two patients with moderately severe right and left ventricular congestive heart failure (Functional Class IV) were studied repeatedly over a period of three to six weeks. One patient (Patient 1) had myocarditis of undetermined etiology and the other (Patient 2) had syphilitic aortic regurgitation. The first subject died two weeks after completion of the last observation (no autopsy obtained), and the other is still living but has remained in Functional Class III. During the entire period of study Patient 1 remained in Functional Class IV, showing only slight variations in the degree of failure. Patient 2 returned to Functional Class III and was in that state for the two final recordings noted in Fig. 2. Both patients were in their most severe state of failure during the initial observations. Patient 2 had a definite exacerbation of her failure during the tenth day of observation.

Fig. 2 summarizes in detail the fluctuations in the various physiologic phenomena recorded. It can be seen that, in the main, there are definite variations in the rates of water and heat losses. It was not until Patient 2 reached a fairly steady state of cardiac function (in Class III) that the observed phenomena became stabilized.

DISCUSSION

It can be seen from the results and especially from Fig. 1 that the rates of water and heat loss from the respiratory tract in congestive heart failure are greater than normal. These increases over the normal are essentially proportional and appear to conform to that which would be expected upon the basis of increased rates of irrigation of the respiratory tract with air (dyspnea) and metabolism. This fact is borne out by the percentage increases in value of the various physiologic phenomena observed. Consult Fig. 1 for the percentage change from the normal in patients with congestive heart failure. A study of Fig. 1 reveals that the increases in water and heat lost from the respiratory tract are more the result of the dyspnea with the resultant increase in the rate of irrigation of the respiratory tract with air than to an increase in the rate of metabolism associated with the congestive heart failure. For example, there was an increase of 25.6 per cent in the rate of irrigation of the respiratory tract with air, 17.7 per cent in the rate of water loss, 19.4 per cent in the rate of heat loss by warming inspired air, and 9.1 per cent in the total amount of heat loss from the respiratory tract. At the same time there was an increase of only 4.8 per cent in heat loss by the excretion of carbon dioxide and 6.7 per cent increase

in the metabolic rate. The rates of water loss and heat loss by convection which depend upon the rate of irrigation of the lungs with air showed the greatest degree of increase over the normal, while heat loss from carbon dioxide excretion, dependent mainly upon the rate of metabolism, showed relatively little increase over the normal. Therefore, the ventilation of the lungs and not metabolism was largely responsible for the differences noted between congestive heart failure and the normal.

As in the normal subjects,[1] there was a high positive correlation between the rate of irrigation of the respiratory tract with air and the rate of water loss, the coefficients of correlation being 0.914 ± 0.014 in the patients with congestive heart failure. These findings are to be expected since the amount of water vapor that might be conveyed away by air is dependent in a large measure upon the amount of air available.

Since the carrying capacity of a unit volume of inspired air was the same in both groups of studies, the possible causes for differences in the rates of water loss between the normal subjects and the patients with heart failure might be due to: (1) the presence of large amounts of free fluid in the alveoli and small bronchioles in the patients with left ventricular failure and pulmonary edema and (2) the dyspnea. All of the patients with heart failure had fine moist râles at the bases of the lungs and all had a moderate amount of dyspnea. None had gurgling râles or were frothing at the mouth and none suffered with severe dyspnea, shock, and marked apprehension. Since the mean relative humidity of the expired air was 88 per cent (extremes, 78 and 96.5) for the normal and 87 (extremes, 74 and 96) for the patients with heart failure, the same amount of water vapor was added to each unit volume of inspired air in spite of the dyspnea and the extra amount of free fluid in the lungs in the patients with heart failure. The surface area of the pulmonary epithelium was probably reduced by the accumulation of fluid in the heart failure patients; but either because of insufficient change in the area or because of an increase of the vapor tension above the edema fluid, the relative humidity of the expired air did not change significantly from normal. The total amount of water lost in left ventricular congestive heart failure via the respiratory tract was 25.6 per cent greater than that for the normal under comparable conditions because of the dyspnea and the resultant rapid rate of irrigation of the respiratory tract with air. Obviously, the rate of heat loss by the vaporization of water follows the same principles and arguments governing water loss just described.

Under similar atmospheric conditions the temperature of the air expired by the normal subjects was 33.2° C. (extremes, 31.6 and 34.2) while the temperature of the air expired by patients with congestive heart failure was 33.0° C. (extremes, 31.1 and 34.2). As in the case of the relative humidity of the expired air, the presence of fluid in the lungs and the dyspnea did not interfere significantly with the warming of inspired air. The rate of heat loss by convection was 27.6 per cent greater in the patients with congestive heart failure, however. This increase was due to the greater rate of irrigation of the respiratory tract with air.

Since the rate of metabolism was only 6.7 per cent greater in the patients with congestive heart failure, and since the excretion of carbon dioxide is mainly dependent upon the rate of metaboblism, the heat loss from the decomposition of carbonic acid in the lungs resulted only in a relatively slight increase in the rate of heat loss by carbon dioxide excretion. Therefore, the greater rate of heat loss (9.1 per cent) in congestive heart failure was due to an increase in the rate of heat loss by vaporization and convection.

The total body heat loss was not determined directly but was estimated by, first, measuring the rate of heat production from the rate of oxygen consumption and, second, assuming that the subject resting for sixty minutes in the comfortable room was in a state of thermal equiiibrium with the environment. It is obvious that such an estimation of total body heat loss is subject to error. This may explain the finding that there was an increase above the normal of 9.1 per cent in heat loss from the lungs with only a 6.7 per cent increase in total body heat loss, a difference of 2.4 per cent. It is more likely, however, that this difference is due in large part to the dyspnea with the associated rapid rate of ventilation of the respiratory tract with air and the resultant increase in heat loss by vaporization of water and convection of heat. Obviously, such a discrepancy could exist for only a short period of time, as during a paroxysm of dyspnea, or there would result an associated decrease in body heat. The nature of the above studies rendered it impossible to evaluate such phenomena.

SUMMARY

A study of the rates of water and heat loss from the respiratory tract of 24 resting sitting patients with right and left ventricular congestive heart failure (Functional Class IV) and living in the subtropical climate of New Orleans showed the following when the room atmosphere was comfortable (temperature, 20.1° C.; relative humidity, 56 per cent):

1. The mean rate of water loss from the respiratory tract was 0.944 Gm. per square meter of body area per ten minutes (extremes, 0.625 and 1.482). When the room temperature was increased from 20.1° C. to 21.5° C., the mean rate of loss was essentially unchanged (mean, 1.052; extremes, 0.694 and 1.456).

2. The mean temperature of the expired air was 33.1° C. (extremes, 31.1 and 34.2). The values were 33.4° C. (extremes, 32.5 and 34.8) when the room temperature was increased to 21.5° C.

3. The mean relative humidity of the expired air was 87 per cent (extremes, 82 and 94). The value became 88 per cent (extremes, 83 and 96) when the room temperature was changed to 21.5° C.

4. The mean rate of irrigation of the respiratory tract with air was 44.929 liters per square meter of body area per ten minutes (extremes, 25.381 and 70.259). When the room temperature was increased to 21.5° C. these values became 48.286 liters (extremes, 37.266 and 74.238).

5. There was a high correlation between the rates of water loss and irrigation of the respiratory tract with air, the coefficient of correlation being 0.934 ± 0.0144.

6. The mean rate of heat loss from the respiratory tract by the vaporization of water, h_e, was 0.553 calorie per square meter of body area per ten minutes (extremes, 0.286 and 0.868). The values became 0.617 (extremes, 0.407 and 0.853 when the room temperature was raised to 21.5° C. This represented 6.55 per cent (extremes, 3.84 and 8.99) of the total heat lost from the body and 54.5 per cent (extremes, 28.2 and 85.7) of the total heat lost from the respiratory tract.

7. The mean rate of heat loss by convection, h_c, or warming inspired air was 0.157 calorie per square meter of body area per ten minutes (extremes, 0.091 and 0.248). The values became 0.157 (extremes, 0.108 and 0.231) when the room temperature was changed to 21.5° C. This represented a mean of 1.85 per cent (extremes, 1.26 and 2.45) of the total heat lost from the body and 15.5 per cent (extremes, 9 and 24.5) of the total lost from the respiratory tract.

8. The mean rate of heat loss by the decomposition of carbonic acid and excretion of carbon dioxide, h_{CO_2}, was 0.305 calorie per square meter of body area per ten minutes (extremes, 0.198 and 0.440). The value became 0.319 (extremes, 0.264 and 0.419) when the room temperature was increased to 21.5° C. This represented 3.63 per cent (extremes, 3.32 and 4.25) of the total heat lost from the body and 30.1 per cent (extremes, 19.6 and 43.4) of the total heat lost from the respiratory tract.

9. The mean total rate of heat loss from the respiratory tract was 1.013 calorie per square meter of body area per ten minutes (extremes 0.631 and 1.830). The values became 1.093 (extremes, 0.796 and 1.503) when the room temperature was increased to 21.5° C. This represented 12.04 per cent (extremes, 8.78 and 14.81) of the total heat lost from the body.

10. The rates of water and heat loss from the respiratory tract of patients with left and right ventricular congestive heart failure (Function Class IV) were definitely greater than the rates observed under similar conditions in 107 normal subjects. These increases were due in a large measure to the dyspnea and associated increased rate of irrigation of the respiratory tract with air. The extra amount of edema fluid in the lungs apparently influenced the results very little. A theoretical discussion of the principles concerned is presented.

An appreciation for the keen interest and significant technical assistance of Mr. G. Morgavi is expressed.

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WOLFF-PARKINSON-WHITE SYNDROME

A Clinical Study With Report of Nine Cases

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THE number of cases reported during the past few years would indicate that the syndrome of a "short PR interval with a prolonged, aberrant QRS complex" occurs much more frequently than has hitherto been realized. The criteria for diagnosis have been modified and the theories which have been advanced in explanation of the findings have become more numerous and involved.

Though the anomaly had been reported previously,[9, 18] Wolff, Parkinson, and White[21] were the first to present a group of cases that illustrated all of the common features. Their original article suggested that increased vagus tone was responsible for the short P-R interval and QRS prolongation. This appeared to be confirmed in those instances in which exercise or the administration of atropine produced a normal electrocardiographic pattern. As has been pointed out,[15] this theory implies a paradoxical effect of vagus tone with a simultaneous exercise of two diametrically opposed influences, one accelerating conduction between auricles and ventricles with shortening of the P-R interval, the other retarding conduction through the bundle of His giving rise to the lengthening and distortion of the QRS complex.

Hunter, Papp, and Parkinson[11] later suggested that the electrocardiographic findings could be explained as being the result of a "fusion beat," on the basis of a "double rhythm" in which the auricular impulse fuses with a beat which arises in one bundle branch. They postulated two centers bearing a constant relationship. The hypothesis explains many of the findings but it is difficult to accept when other simpler mechanisms based on anatomic findings and experimental demonstrations are available. Also, as has been demonstrated, premature auricular beats may be followed by the usual distorted QRS complex.[20]

The most satisfactory explanation to date was initially advanced by Holzmann and Scherf in 1932[10] and by Wolferth and Wood in 1933,[19] and is based on the hypothesis of an accessory pathway of A-V conduction with ventricular asynchronism as a result of the premature stimulation of one ventricle.

The existence of accessory neuromuscular connections between the auricles and ventricles was demonstrated by Kent in 1914[12] and by Glomset and Glomset in 1940.[7] In 1943, Wood, Wolferth, and Geckeler,[22] through serial microscopic sections of the auriculoventricular groove, were able to identify a "Bundle of Kent" in the heart of an individual who, during life, showed the anomaly of a short P-R interval and a prolonged QRS complex with paroxysmal tachycardia.

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The interesting experimental work of Butterworth and Poindexter[1, 2] has added further weight to the theory that an accessory pathway is responsible for the phenomena observed in this syndrome. By means of an electrical amplifier the impulses from the auricle were conducted to one ventricle before they were conducted to this ventricle normally through the auriculoventricular conduction system. This produced typical electrocardiographic tracings with a short P-R interval and QRS prolongation. Reversal of the electrical stimulus from ventricle to auricle resulted in auricular tachycardia.

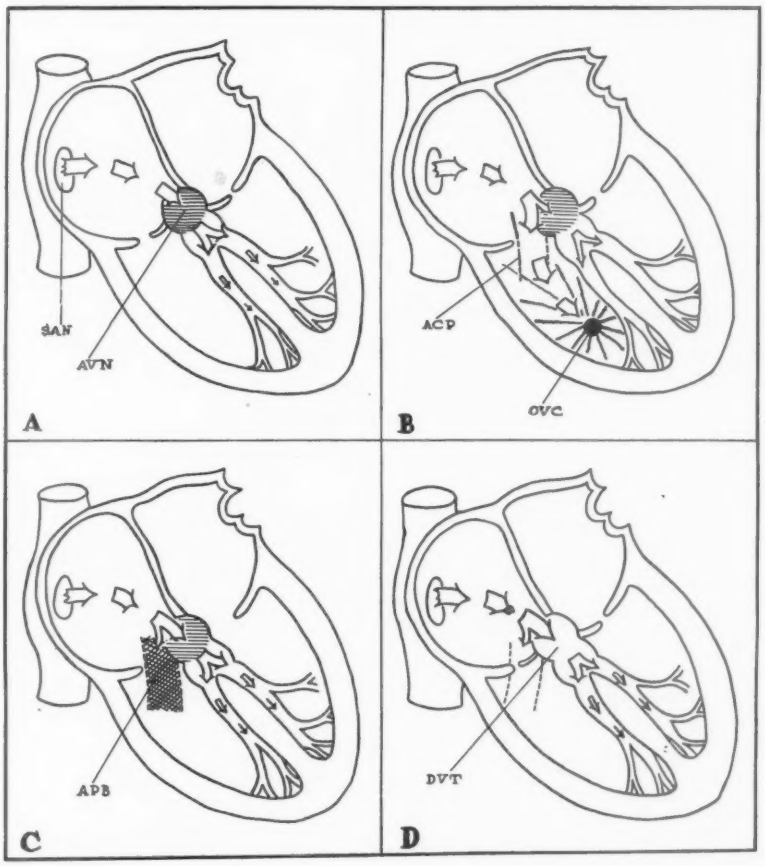

Fig. 1.—*A*, Diagrammatic representation of the normal origin and conduction of the cardiac impulse. *SAN*, sinoauricular node. *AVN* auriculoventricular node, with normal delay indicated. *B*, Theoretical conduction in Wolff-Parkinson-White syndrome. *ACP*, accessory conduction pathway. *OVC*, origin of ventricular contraction. *C*, Condition which obtains with use of quinidine. *APB*, accessory pathway blocked. *D*, Condition present following the use of atropine. *DVT*, diminished vagus tone.

The simple hypothesis of an accessory A-V pathway has always left much to be desired in the explanation of the Wolff-Parkinson-White syndrome. With the study of "fusion beats" by Butterworth and Poindexter,[3] we have an important contribution to the better understanding of the mechanisms involved. Their work supports the supposition that an auricular impulse may travel down

both the A-V bundle and an accessory pathway and result in a "fusion beat." The QRS configuration is determined by the degree of fusion which in turn is dependent upon the speed of conduction in each channel and the relative proximity of these channels to the initiating impulse. These authors demonstrated that the ventricle can be stimulated through the normal conduction system and by a second ventricular stimulus only during the short period (approximately 0.08 second) prior to the time the normal QRS complex would ordinarily appear.

It has been repeatedly pointed out that the Wolff-Parkinson-White syndrome occurs most commonly in young healthy adults. Many authors reporting instances in which myocardial damage was very likely or possibly present have made it a point to disregard or minimize that feature. In more recent years a few articles have appeared in which the presence of myocardial pathology is stressed.[6, 8, 14] In reviewing our own cases and those in the literature we have been struck with the fact that no cases have been reported in infants, that a number of cases showing the Wolff-Parkinson-White syndrome have subsequently lost all evidence of it,[19, 21] and that many published electrocardiograms indicate obvious myocardial disease. Though we are at a loss to explain the connection, it would appear that the presence of disease is more than a coincidence. Hunter and his associates[11] thoroughly reviewed the literature and found that, of ninety cases reported, eighteen had evidence of cardiac disease. They remarked that the syndrome undoubtedly could be produced by heart disease but pointed out that the presence of a short P-R interval with QRS distortion in no way influenced the prognosis. They noted that the syndrome was found associated with mitral stenosis, hypertension, aortic insufficiency (syphilitic and rheumatic), coronary thrombosis, and thyrotoxicosis. The oldest patient reported was 62 years of age. Wolferth and Wood[19] reported the syndrome in a child of 14 who had a history of recurring paroxysmal tachycardia from the age of 2 years.

We are reporting nine cases that illustrate some of the variations encountered. They came to our attention during a period of one year in which approximately 3,600 electrocardiograms were reviewed.

REPORT OF CASES

CASE 1.—A 36-year-old white soldier came into the hospital on Dec. 2, 1944, because of shortness of breath and a "fluttering" sensation in the chest. There had been two previous episodes of dyspnea and tachycardia within the preceding three years, each lasting six to seven days. Although there was a history of some shortness of breath since childhood, this apparently did not interfere with his customary activities. The family and past history were noncontributory.

The heart was not enlarged. No murmurs were present. The heart rate was 120 at the wrist and approximately 130 at the apex. The rhythm was totally irregular. The lungs were clear. A soft mass, the size of a hazelnut, was noted in the left lobe of the thyroid. The examination was otherwise normal.

Vital capacity, circulation time, blood, urine, and x-ray studies of the heart were all normal. The basal metabolism was -10.

The patient was digitalized, and by the following morning the rhythm was regular with a rate of 86 per minute. The sounds were of good quality and no murmurs or thrills were noted. Digitalis was omitted the second day and, except when used experimentally later, was not again employed. During the two months that he was observed there were no other episodes of tachycardia or arrhythmia and no other cardiac symptoms.

Comment.—This was a case which demonstrated auricular fibrillation with persistence of the abnormal ventricular pattern indicating that the distribution was largely via the accessory pathway. It strongly resembles Case 1 of Levine and Beeson's[13] series which was interpreted as ventricular tachycardia. During both spontaneous and induced (quinidine) reversion to normal distribution, T_2 and T_3 became sharply inverted resembling in appearance the curves seen in myocardial disease. Varying degrees of fusion could be produced with quinidine.

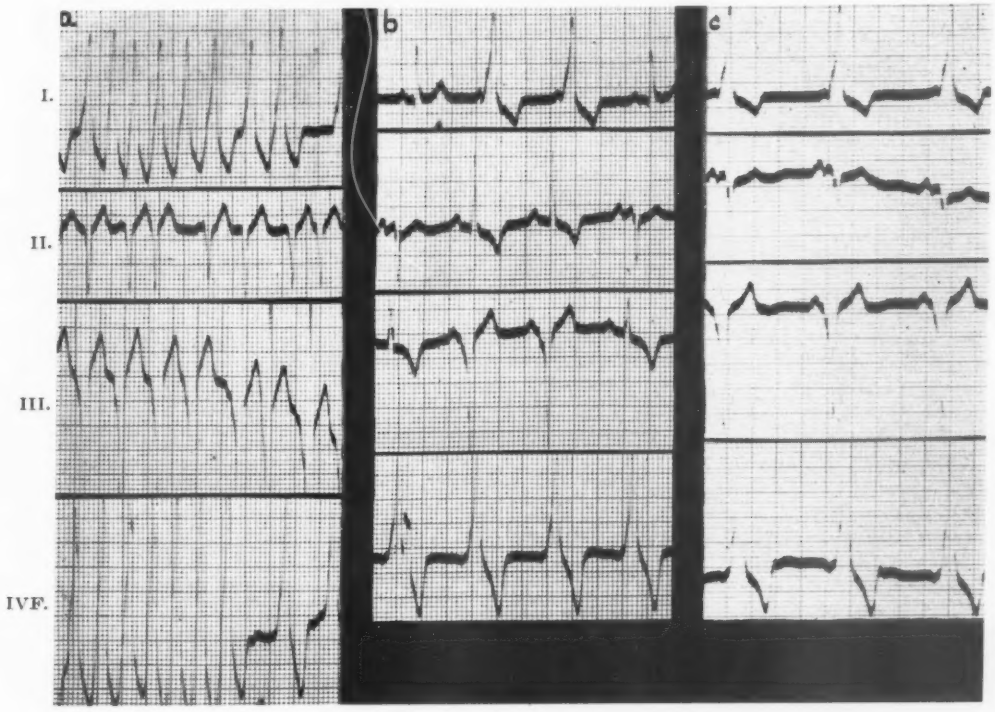

Fig. 2.—Case 1. *A*, Auricular fibrillation with a ventricular rate varying between 210 and 340 per minute. Duration of QRS approximately 0.12 second. Left axis deviation. *B*, This graph, made following cessation of tachycardia, demonstrates a mixture of normal and aberrant complexes. The normal complexes (Beats 1 and 4 in Lead I, Beats 2 and 3 in Lead II, and Beat 4 in Lead III) have a P-R interval of 0.16 second and a QRS duration of 0.06 second with an upright T_1 and sharply inverted T_2 and T_3. The aberrant complexes have a P-R interval of 0.06 second and a QRS duration of 0.14 second and demonstrate left axis deviation. The P-S intervals of the normal and abnormal beats are identical. *C*, All of the complexes are typical of those seen in the Wolff-Parkinson-White syndrome. Measurements and contour of the complexes are essentially the same as those of the abnormal beats in *B*.

Case 2.—A 26-year-old white soldier came into the hospital on March 11, 1945, with a complaint of "rapid beating of the heart." During the preceding three years he had been subject to fairly frequent episodes of typical paroxysmal tachycardia which required no treatment. When seen by the admitting officer, the pulse was found to be between 170 and 180 per minute, but by the time an electrocardiogram was made the rate was well within normal limits.

Physical examination revealed a healthy looking young man who was completely comfortable. The heart was entirely normal on examination. X-ray films of the chest showed no evidence of cardiac enlargement. The vital capacity, circulation time, and all cardiac function tests were normal. While under observation the patient had no cardiac complaints nor did he experience any further attacks of tachycardia.

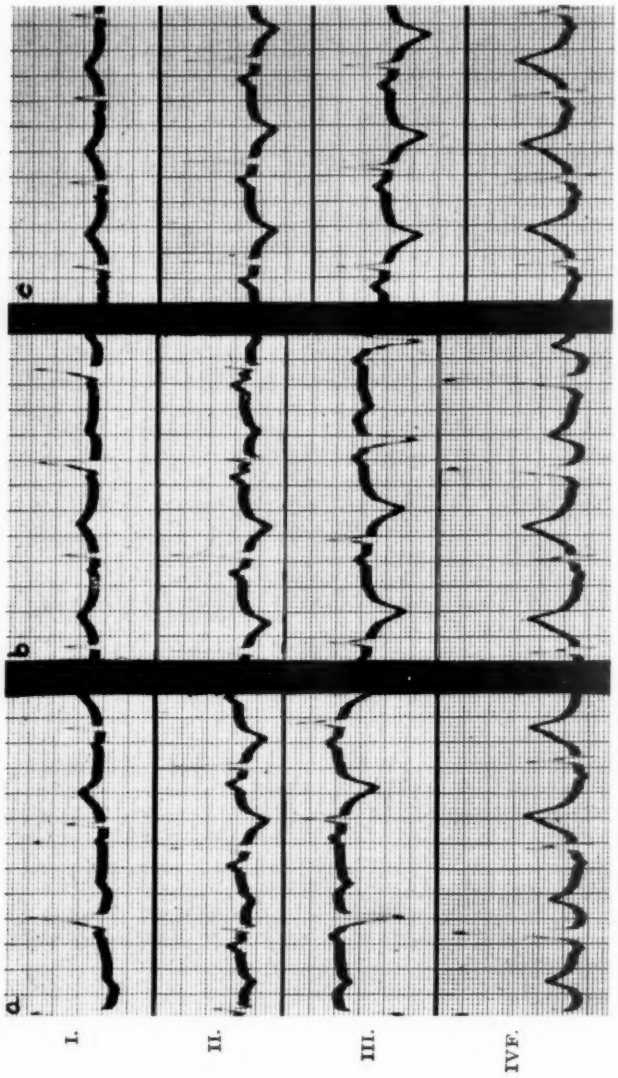

Fig. 3.—Case 1. *A*, This curve was obtained during the administration of quinidine (24 grains in two and one-half hours) and demonstrates not only a change to comparatively normal complexes but also an intermediate form (Beats 1 and 2 in each lead) first noted after the administration of small doses of the drug. In these beats the short P-R, long QRS relationship is maintained but alterations have occurred in the T waves and in QRS_2. These beats are transitional in character and probably represent varying degrees of fusion. The third and fourth beats in each lead indicate normal conduction and are essentially the same as those in *C* which occurred spontaneously. *B*, This tracing demonstrates the inherent instability of the state produced by inadequate quinidine dosage. Reversion to abnormal conduction is noted in Beats 3 and 4 of each lead. *C*, This tracing is representative of results obtained at will in Case 1 by adequate quinidine dosage. The P-R intervals are 0.16 second and the QRS complexes are 0.07 second in duration. T_2 and T_3 are inverted. The axis is normal.

Comment.—Although no paroxysmal tachycardia was recorded, this appears to be a typical case of the Wolff-Parkinson-White syndrome. Normal conduction could be obtained with quinidine, and intermediate forms were recorded with atropine and atropine with exercise.

CASE 3.—A 32-year-old white soldier was admitted on Jan. 2, 1945, with complaints of diarrhea and abdominal pain. There were no cardiac symptoms.

Physical examination was entirely unremarkable with the exception of some evidence of moderate weight loss and dehydration. The heart was within normal limits. An x-ray film of the heart was normal. All cardiac function studies were normal. Stool examination revealed trophozoites of *Endamoeba histolytica* and the diagnosis of amebic dysentery was made. Before beginning treatment with emetine, an electrocardiogram was made and found to be abnormal (Fig. 5a).

During the period of hospitalization this patient exhibited no paroxysmal tachycardia and had no cardiac complaint of any character.

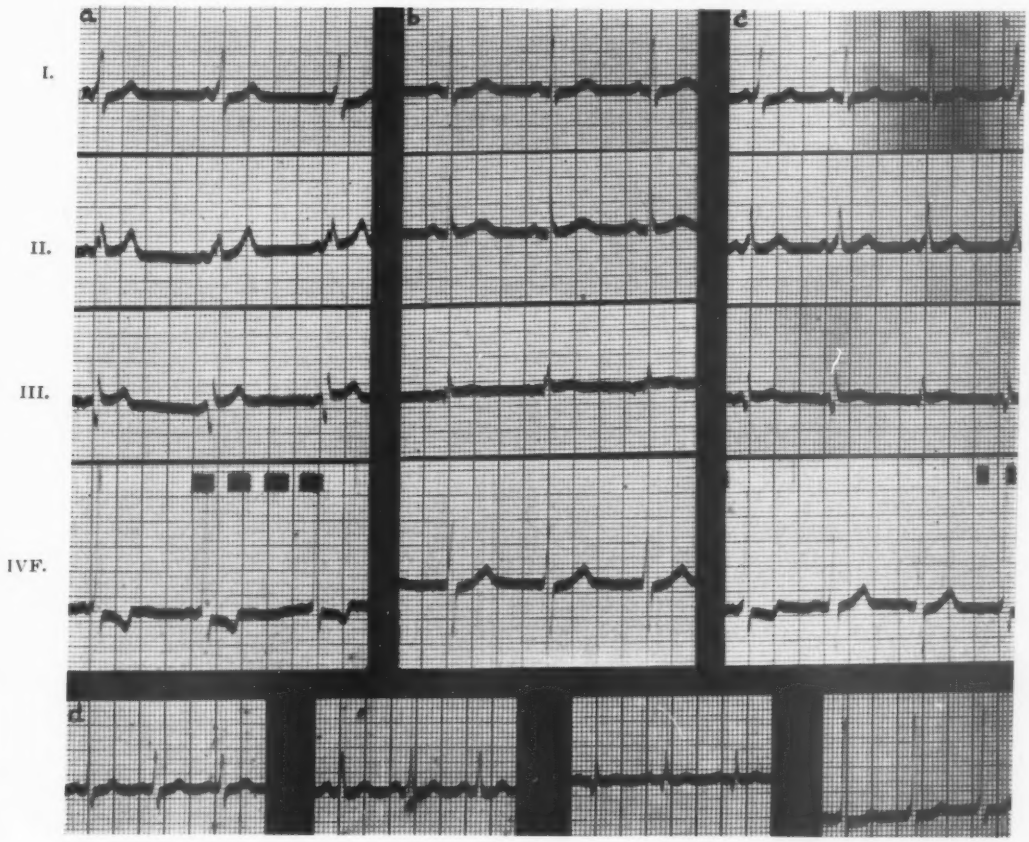

Fig. 4.—Case 2. *A*, Obtained on admission. P-R intervals 0.08 second. QRS duration 0.12 second. Slurring of the initial stroke of the QRS wave. Deep Q_3. Left axis deviation. *B*, Recorded after the administration of quinidine (24 grains in six hours). P-R intervals 0.14 second. QRS duration 0.07 second. Normal axis. *C*, Made after the intravenous administration of atropine (1/37 grain). Some of the complexes (the first beat in Lead I, all beats in Lead II, Beats 1 and 2 in Lead III and Beat 1 in Lead IV) are intermediate between those demonstrated in *A* and *B* and represent varying degrees of fusion. P-R 0.10 second. QRS 0.10 second. Axis normal. T_4 diphasic. *D*, Made after intravenous atropine and exercise. Except for the rate this curve is very similar to *B*. However, note upright P_3 (inverted in other tracings).

Comment.—This patient never had paroxysmal tachycardia or any other cardiac complaint. Although varying degrees of "fusion" could be produced with the administration of quinidine and atropine, the electrocardiographic pattern could not be brought back to normal.

CASE 4.—A 29-year-old soldier came into the hospital on Dec. 6, 1944, with a complaint of attacks of rapid heart action accompanied by shortness of breath. He had been receiving antisyphilitic therapy. Because of a positive spinal fluid Wassermann, he was transferred to an appropriate installation for definitive treatment, but was returned to the original station because of an abnormal electrocardiogram.

Physical examination was not remarkable. The heart was not enlarged, the rate was moderate, the rhythm was regular, and the sounds were good. No murmurs or thrills were noted. The lungs were clear and resonant throughout, and the reflexes were normal. All laboratory studies and cardiac function tests were within normal limits.

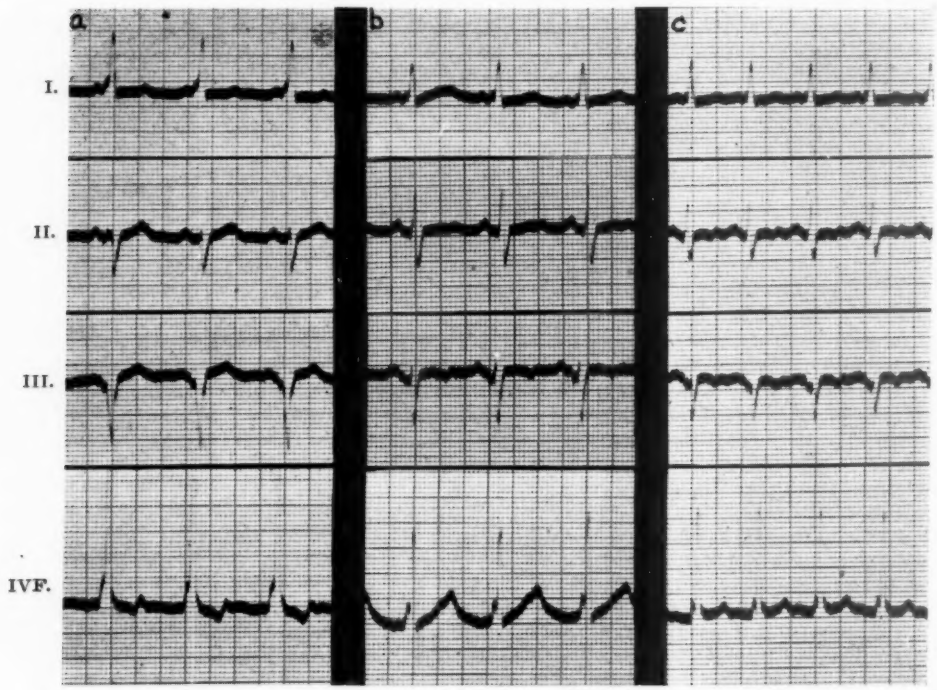

Fig. 5.—Case 3. *A*, Obtained on admission. P-R, 0.08 second. QRS, 0.14 second. Left axis deviation. *B*, Taken after the administration of quinidine (24 grains in three hours). P-R and QRS are difficult to measure but are probably not appreciably altered. There is a change in the axis with the appearance of a large R_2 and a small R_3 and diminution in the depth of S_3. T_1 is higher, T_2 is lower, and T_3 is inverted. A large T_4 is noted. *C*, Recorded following the administration of atropine.

The patient continued to receive antisyphilitic therapy while on the cardiac ward. Six or seven hours after one such treatment he complained of a fluttering sensation in the chest and of breathlessness. This attack persisted for about one hour and toward its conclusion it was noted that the pulse was irregular.

During the two months that this soldier was under observation there were no instances of definite paroxysmal tachycardia and no cardiac symptoms.

Comment.—The tachycardia in this case is rather slow to be considered paroxysmal in character. Furthermore, the short P-R, wide QRS relationship persists. The significance of this is not clear.

Of considerable interest is the appearance of normal QRS complexes following sinus pauses. This is taken to indicate that since these ventricular com-

plexes were the result of impulses originating in or in the close vicinity of the A-V node, transmission distal from that point was in a normal fashion and did not involve the accessory pathway.

CASE 5.—A 37-year-old white soldier was hospitalized on May 23, 1945, because of frequent attacks of rapid heart action during the three weeks prior to his admission. The

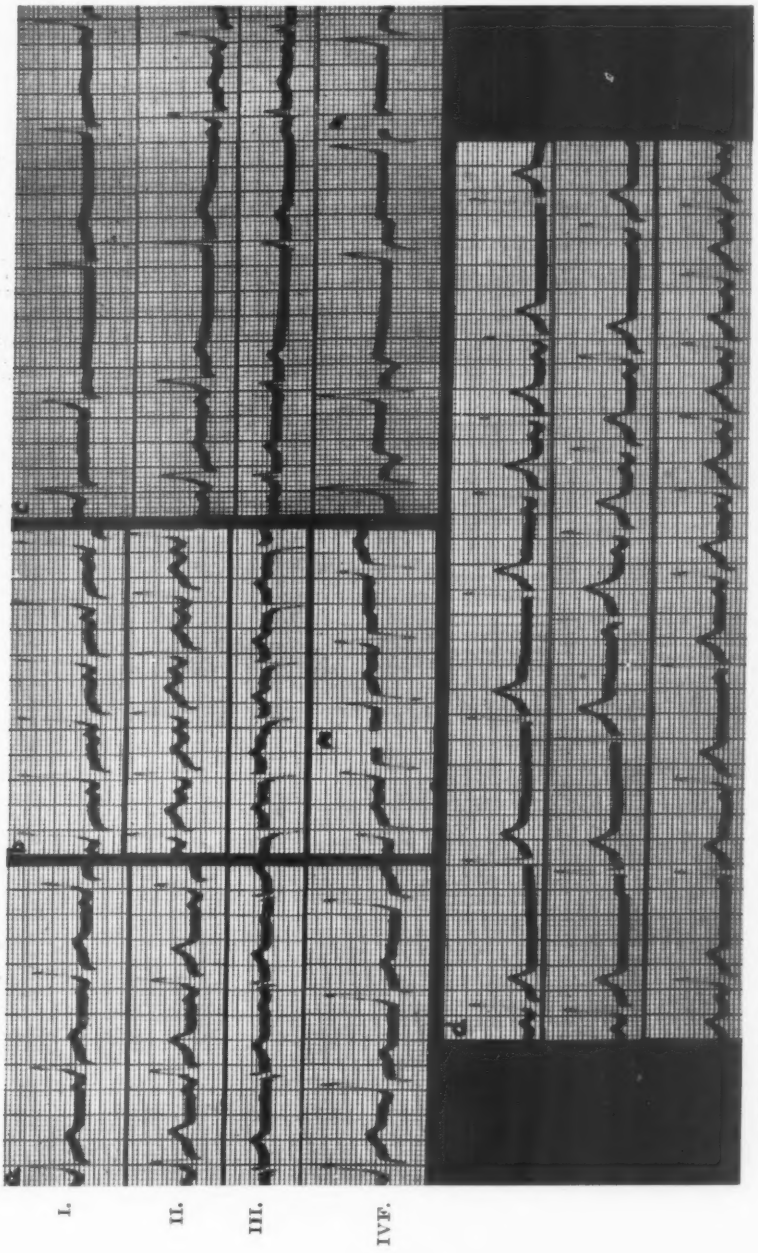

Fig. 6.—Case 4. *A*, On admission, P-R, 0.12 second. QRS, 0.13 second. Slurring of the initial limb of the QRS complex. Axis normal. T waves upright in all leads. *B*, Taken after the administration of mapharsen. Rate 130. P-R, 0.10 second. QRS, 0.12 second. Appearance of deep Q_3. Left axis deviation. Diminution in height of T_1 and T_4. *C*, Following quinidine. Note inversion of T_1 and T_4 with changes in rhythm and conduction. QRS complexes of normal contour and duration (0.07 second) are observed following periods of sinus pauses. *D*, All are Lead II, obtained during an interval of irregularity that followed the administration of mapharsen. There are periods of sinus pauses with nodal escape similar to those noted in *C*.

first attack came on suddenly three years earlier. Greater physical activity encountered in the Army was apparently responsible for the increasing frequency of the episodes. There were no other cardiac symptoms and no complaints of any kind between attacks of tachycardia.

Physical examination was entirely unremarkable with the exception of a soft systolic murmur which was best heard over the apex. The pulse was slow and regular. The heart was not enlarged. The lungs were clear. All the laboratory procedures and cardiac function tests were found to be normal.

Following a long period of observation, we were able to obtain a tracing during a paroxysm of tachycardia. This was controlled by breath holding.

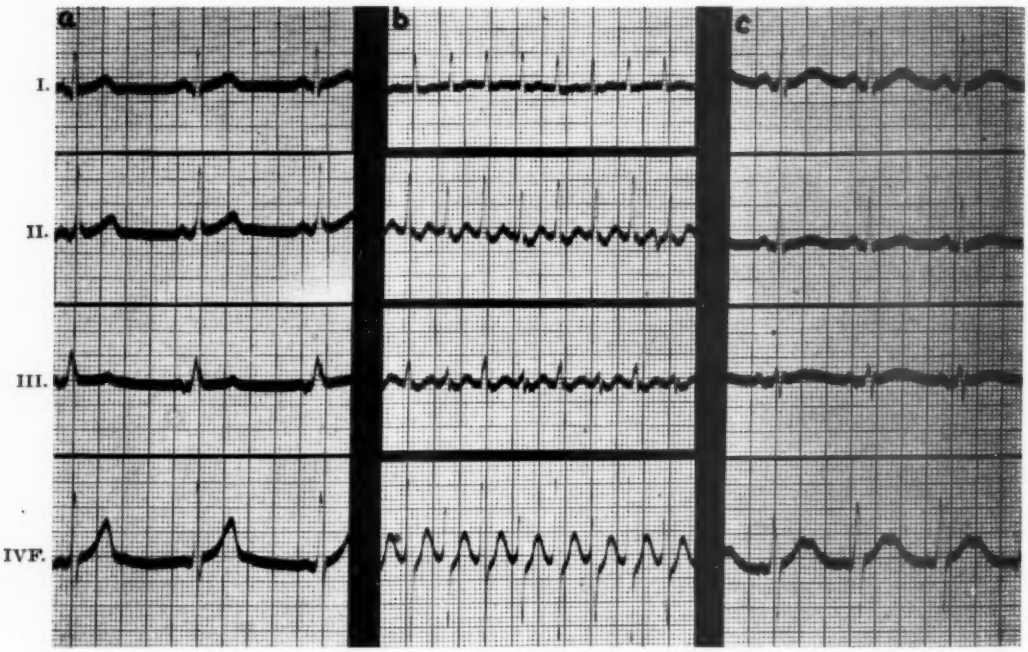

Fig. 7.—Case 5. *A*, Obtained on admission. P-R, 0.10 second. QRS, 0.12 second. Axis normal. *B*, Obtained during a paroxysm of tachycardia. Rate 210. Rhythm probably paroxysmal nodal tachycardia. P waves are not identifiable. QRS, 0.06 second. Axis essentially unaltered. Electrical alternans noted. *C*, Made following administration of quinidine (24 grains in three hours). P-R, 0.14 second. QRS, 0.08 second. Slight left axis deviation. T waves lowered, rounded, prolonged, and notched due to quinidine effect.

Comment.—The diagnosis in this case was obscure because accurate measurement was difficult. Additionally, the axis was normal. The use of quinidine produced changes which were definite though not spectacular. The record obtained during the paroxysm of tachycardia confirms the diagnosis. Rather marked electrical alternans appeared during the tachycardia.

CASE 6.—A 30-year-old soldier came into the hospital on June 12, 1945, with the complaint that his heart occasionally "skipped a beat." On rare occasions, ever since childhood, he also is said to have had short periods of rapid heart action. The only other complaint referable to the heart was that of dyspnea on moderate exertion. During a previous hospitalization a diagnosis of heart block was said to have been made.

On physical examination the heart was not enlarged, the rate was moderate, the rhythm was regular, and the sounds were good. No murmurs or thrills were noted. A rare extrasystole was observed. X-ray films of the chest were normal and all cardiac function tests and laboratory procedures were within normal limits.

During the period of hospitalization there were no episodes of tachycardia and no cardiac symptoms.

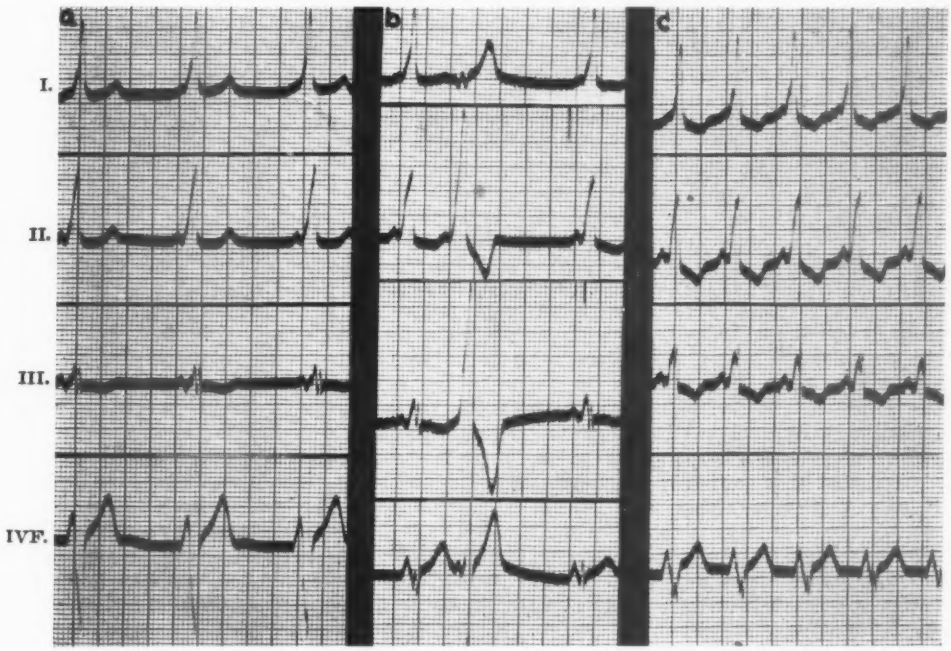

Fig. 8.—Case 6. *A*, Recorded on admission. P-R, 0.08 second. QRS, 0.16 second. Initial deflection of R wave is slurred. Axis normal. *B*, Ventricular extrasystoles are present. Premature beats were never observed except following exercise and were always associated with depression or inversion of the T waves in the limb leads. *C*, This tracing was obtained following vigorous exercise. Rate, 116. P-R, 0.10 second. QRS, 0.10 second. T waves sharply inverted in all limb leads and S-T segments slightly depressed. There is diminution in the size of all waves in Lead IV.

Comment.—This case is of interest in that ventricular premature beats were recorded. They occurred following slight exercise and were abolished during greater activity.

The same case presented a phenomenon which to us is without adequate explanation. Electrocardiograms made following brisk exercise always demonstrated inversion of the T waves in the limb leads and diminution in height of all the waves in Lead IV. There was also a slight increase in the P-R interval and a shortening of the duration of the QRS complex.

CASE 7.—A 28-year-old white soldier entered the hospital complaining of a generally tired-out and run-down feeling. The family and past history were noncontributory. Approximately six years earlier, he was examined for life insurance and hypertension was noted. He tired rather easily on moderate effort and suffered from occasional occipital headaches. There was no dyspnea on exertion nor precordial distress and no edema of the extremities was ever noted.

Physical examination was not remarkable. The heart was not enlarged, the rate was moderate, the rhythm was regular, and the sounds were of good quality. No murmurs or thrills were noted. The blood pressure was 150/92. X-ray films of the heart demonstrated no enlargement or distortion. The lungs were normal. The serology was negative and all other laboratory findings were normal. The cardiac function tests were normal.

During his hospitalization the patient did not have any tachycardia nor were there any other complaints referable to the heart.

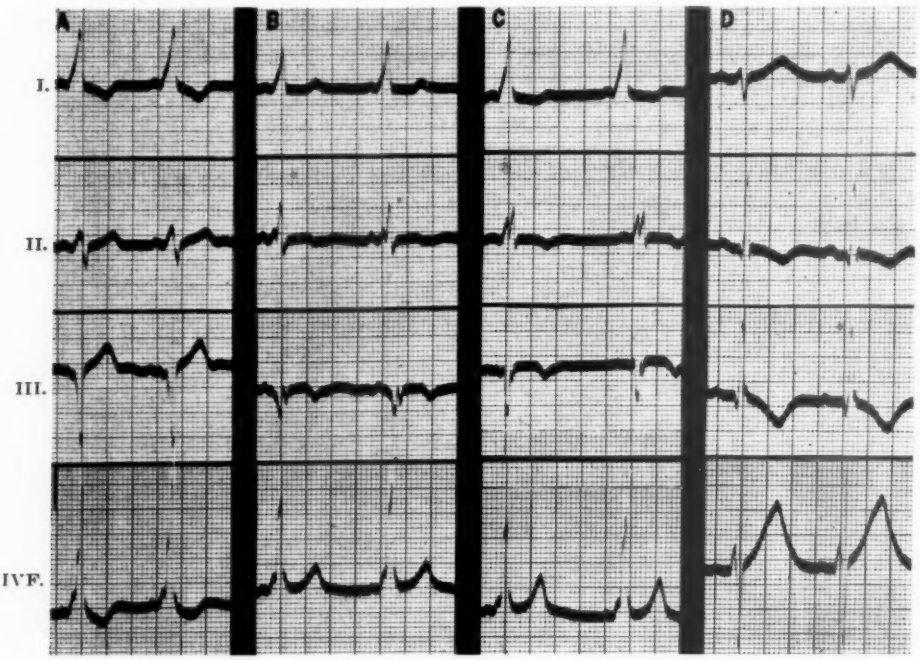

Fig. 9.—Case 7. *A*, Recorded on admission. P-R, 0.10 second. QRS, 0.14 second. Left axis deviation. The T waves are inverted in Leads I and IV, and upright in Leads II and III. *B*, This tracing was obtained several hours after that shown in *A*, and under identical circumstances. P-R and QRS durations are unchanged. There is marked alteration in the appearance of QRS complexes of Leads II and III. RS-T_1 is somewhat depressed. T_1 is upright, T_2 is diphasic, and T_3 is inverted with rounded and slightly elevated RS-T segments. T_1 has become erect. *C*, This tracing was obtained under the same conditions that obtained in *A* and *B*. No medication had been given. Duration of P-R and QRS unchanged. Configuration of QRS_2 has altered. T_1 is diphasic, and T_2 and T_3 are inverted. RS-T_3 is elevated. Lead IV is unchanged. *D*, This tracing was made approximately one hour after the administration of 33 grains of quinidine. P-R, 0.18 second. QRS, 0.10 second. There is slight right axis deviation with a small R_1 and prominent S_1. The T waves are all large and rounded. T_1 is upright, T_2 and T_3 are sharply inverted. QRS_1 has acquired a deep S wave while the height of the R wave has decreased. This tracing strongly resembles that obtained in Case 1 by similar means (Fig. 3, *C*).

Comment.—This patient is of considerable interest because of the marked alterations in the appearance of the ventricular component which occurred spontaneously and under unvarying circumstances. This change cannot be explained on the basis of altering degrees of fusion because the P-R intervals and the QRS duration remain constant and unchanged. The only satisfactory explanation which can support these findings is that of *multiple* accessory pathways.[17] Under such circumstances, variation in the number and/or combinations of such channels acting over a given interval could effectively alter the distribu-

tion of the impulse and, with it, the character of the ventricular complex. The factors tending to influence the selection of abnormal pathways are quite beyond our knowledge at the present time. However, they may be susceptible to experimental analysis similar to that employed by Butterworth and Poindexter.[3]

Administration of 33 grains of quinidine over a period of two hours produced characteristic alteration in the appearance of the tracing with reversion to physiologic conduction.

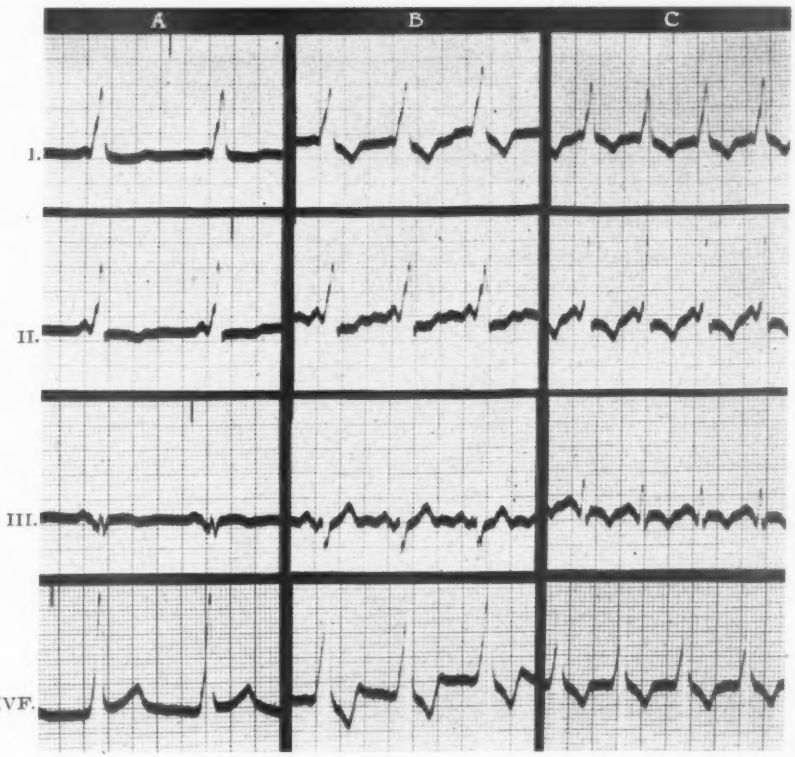

Fig. 10.—Case 8. *A*, Obtained on admission. P-R, 0.08 second. QRS 0.14 second. *B*, Recorded following moderate exercise. Note marked change in the T waves and in the RS-T segments. There is also a shift of the axis toward the left. *C*, Obtained following the intravenous administration of atropine and subsequent exercise. All of the T waves are now inverted. The duration of the QRS complex has been diminished by approximately 0.02 second without a comparable increase in the P-R interval. The axis has rotated toward the right.

CASE 8.—A 26-year-old white soldier came into the hospital on Dec. 11, 1945, complaining of restlessness and rapid, irregular heart action. This occurred suddenly following a brisk run of some 50 yards. The admitting physician described a grossly irregular rhythm and noted a pulse deficit. An electrocardiogram was not made unitl the following morning at which time the arrhythmia had disappeared. The tracing demonstrated a normal rhythm with a configuration characteristic of the Wolff-Parkinson-White syndrome.

The attack for which the patient entered the hospital was his first. The history was otherwise noncontributory. The physical examination revealed only a soft systolic apical murmur. All of the routine laboratory tests, cardiac function tests, and chest x-rays were normal.

The use of quinidine did not alter the tracing significantly but exercise and exercise with atropine resulted in interesting changes.

During his hospitalization the patient had no further attacks of tachycardia and did not have any cardiac complaints.

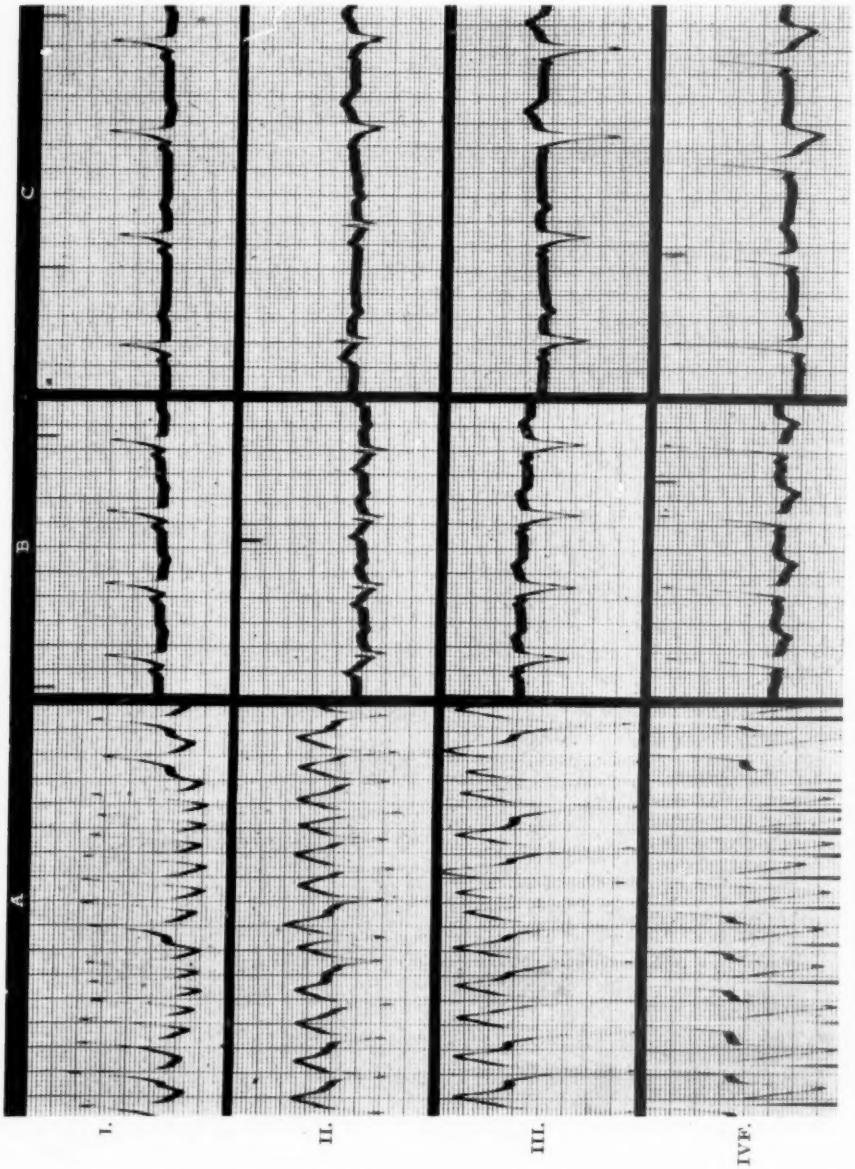

Fig. 11.—Case 9. *A*, Obtained on admission. Rhythm either auricular fibrillation with abnormal ventricular conduction or paroxysmal ventricular tachycardia with marked irregularity. Rate varies between 250 and 300. *B*, Recorded the morning following admission. P-R, 0.10 second. QRS, 0.12 second. Left axis deviation. *C*, This tracing was made several days after *B*. With each lead the patient began in the right lateral position and then turned to the supine. Several seconds and about five beats after the change of position an abrupt change in the appearance of the electrocardiogram occurred. Two beats are shown before and two after the change took place. Note that a change in axis has occurred toward the left and that all of the T waves have reversed their directions.

Comment.—The variations in the axis and in the T waves are probably the result of varying combinations of the several aberrant conduction pathways apparently present in this case. The shortening of the duration of the QRS complex without a like increase in the P-R interval, however, is without adequate explanation.

CASE 9.—A 20-year-old white man was admitted to the hospital on Dec. 18, 1945, with the complaint of rapid and irregular heart action. There was a history of two similar attacks, both following effort, during the preceding ten years. The history was not otherwise remarkable.

Physical examination revealed the presence of what was apparently auricular fibrillation. The heart was not otherwise unusual and no other abnormalities were observed. An electrocardiogram demonstrated what was either paroxysmal ventricular tachycardia with considerable irregularity or auricular fibrillation with bundle branch block and an exceedingly rapid ventricular rate.

The attack stopped spontaneously during the night and on the following morning the cardiac rate was moderate and the rhythm regular. An electrocardiogram at this time demonstrated a characteristic short P-R, long QRS relationship.

All of the customary laboratory studies were normal. X-ray of the chest and cardiac function tests were all within normal limits.

It was not possible to produce any significant alterations of the electrocardiogram by the use of exercise, atropine, or quinidine. However, a rather unusual electrocardiographic phenomenon was observed in this patient after he had changed his position from right lateral to supine. Several seconds after the change was completed there was an abrupt shift in axis and all of the T waves reversed their direction. That this was not due purely to the anatomic change in position is apparent when it is recalled that there was a delay of several seconds before the electrical change occurred.

Comment.—The tachycardia in this case is probably of the same type as that found in Case 1. It disappeared spontaneously. The immediate cause for the gross changes noted with alteration of anatomic position is not apparent. However, the mechanism is doubtless similar to that postulated in Cases 6, 7, and 8.

DISCUSSION

Several details of this condition merit somewhat further discussion and theory. It has usually been considered that the attacks of paroxysmal tachycardia so frequently associated with this syndrome are the result of impulse re-entry through the anomalous A-V bundle. Since most of the tachycardias recorded are of the supraventricular type with a normal QRS complex it is probable that the original impulse in such instances travels from the auricle down the normal A-V pathway and returns to the auricle through the aberrant channel. The inability of the "Kent bundle" to transmit retrograde impulses would explain the freedom from paroxysmal tachycardia noted in approximately 25 per cent of the reported cases.

In reviewing those cases which were considered to be ventricular tachycardia[13, 16] it is felt that some of the electrocardiograms shown might have been interpreted as auricular fibrillation with a prolonged, distorted QRS similar to Cases 1 and 9 herein reported. In order to explain the wide, bizarre QRS complex, it is necessary to postulate that the path of distribution is largely through the accessory bundle. The cases of true ventricular tachycardia probably arise in the lower portion of the aberrant pathway.

An investigation of this subject by Rosenbaum and his co-workers[17] recently appeared in the JOURNAL. We were interested to find that their deductions, arrived at through careful studies with unipolar leads from the esophagus, precordium, and other parts of the thorax, closely resemble the experimental con-

clusions of Butterworth and Poindexter.[3] They do not employ the term "fusion beats" but conclude that "impulses" pass from the auricles to the ventricles not only by way of the atrioventricular node and His bundle but by "one or more additional channels." They also suggest that these pathways may be present but not functioning. These conclusions appear valid when applied to those cases showing a mixture of abnormal and physiologic complexes (Case 1) and where the abnormal complexes vary in appearance (Case 4).

If the presence of one or more conduction pathways is conceded, the pharmacologic action of quinidine and atropine become apparent. Quinidine by its depressant action on ectopic tissue is thought to delay conduction in the aberrant system thus permitting the impulse to progress down the normal pathway (Fig. 1, *C*). Atropine, on the other hand, by diminishing or abolishing normal or increased vagus control over the A-V conduction system makes the normal pathway the more favorable one and allows the impulse to take that route in preference to the accessory pathway (Fig. 1, *D*). One may liken the two (or more) pathways to competing electrical circuits having different and varying resistances, with the impulse mostly or wholly traversing the one with the least impedance.

Since the pharmacologic action of quinidine and atropine in this condition is apparently complementary, the one interfering with abnormal conduction and the other enhancing physiologic conduction, the two drugs were used simultaneously in those cases not altered by either drug separately. However, it was noted that where quinidine alone did not induce normal conduction the addition of the other drug resulted in no further change. The dose of quinidine required to produce physiologic conduction varied from 6 grains an hour for two or three doses to 33 grains in two hours (Case 7). Atropine in intravenous doses up to $\frac{1}{50}$ grain and atropine with exercise were also effective to a lesser degree. We were unable to obtain satisfactory results with digitalis even though large doses were employed. In Case 1 the rhythm changed from auricular fibrillation to normal either because of or in spite of digitalis.

It is interesting to note that in those cases where physiologic tracings were obtained following the use of quinidine (Cases 1, 2, and 5) the history indicated a fairly recent origin or paroxysmal tachycardia. In Case 7 changes were secured by similar means but this patient had no cardiac complaints. One may speculate that electrocardiographic reversal by pharmacologic means is more likely to occur in those cases where the aberrant mechanism is not one of long standing. In borderline cases it may be possible to employ quinidine as a diagnostic test.

The relationship of myocardial disease to the Wolff-Parkinson-White syndrome is, in our opinion, the major unexplained issue. It is generally admitted that the syndrome may be produced occasionally by heart disease. Case 1, which showed deep inversion of T_2 and T_3 when the conduction was physiologic suggests that myocardial disease may have had some part. This factor should not be lost sight of, and the nature of the cause, if it can be determined, should always be carefully considered in making a prognosis. A few attractive theories

have been advanced, but no conclusive evidence has been presented. Fox[4] has suggested that a circulatory difficulty of the A-V node due to coronary sclerosis may sufficiently depress its functional activity to permit an already present ectopic mechanism to take over some of the conducting functions. Other inflammatory, toxic or degenerative processes could conceivably have a similar effect. It is our opinion that this phase of the problem has not been sufficiently emphasized or investigated.

SUMMARY AND CONCLUSION

1. Nine patients who showed the Wolff-Parkinson-White Syndrome are presented and a few of the variations encountered are discussed.

2. The various theories advanced in the explanation of the pathogenesis are referred to and an evaluation of their merits is attempted. In our opinion the most acceptable explanation is that which assumes the presence of one and frequently several accessory conduction pathways which result in "fusion beats."

3. The influence of quinidine, atropine, and exercise on the "short P-R, long and aberrant QRS" is discussed. In borderline cases these changes may be employed as a diagnostic test.

4. The relationship of myocardial disease to the Wolff-Parkinson-White syndrome is discussed. Several of the patients reported in this paper had systemic disease and two showed definite electrocardiographic abnormalities during periods of normal conduction.

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Clinical Reports

TRANSIENT VENTRICULAR FIBRILLATION

Report of a Case With Spontaneous Recovery

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IT HAS been fairly well recognized in recent years that cardiac syncope may result from transient ventricular standstill or ventricular fibrillation. Ventricular fibrillation in man is often a terminal event in various forms of cardiac failure, particularly sudden occlusion of the coronary vessels.[1, 2] It has been shown by several investigators,[3-9] particularly Schwartz and Jezer,[6] that ventricular fibrillation may occur as a transient disorder from which the patient may recover. Until the studies of these authors, little was known of the clinical manifestations of this disorder.

Schwartz[4] pointed out that the periods of unconsciousness in patients with auriculoventricular dissociation are associated with transient seizures of ventricular fibrillation much more commonly than had been suspected. He called attention to the fact that the clinical diagnosis of transient ventricular fibrillation may be suspected in such patients if, preceding a period of unconsciousness, the heart rate has been noted to increase above the usual basic rate. Schwartz and Jezer[6] also presented a patient in which certain premonitory disturbances preceded a transient seizure of ventricular fibrillation. One such disturbance consisted of alternate premature beats of the ventricles, which increased the basic ventricular rate. These were followed shortly by irregular periods of recurring groups of aberrant ventricular oscillations, of which only the first few could be heard at the apical region of the heart or felt at the radial pulse. Borg and Johnson[7] presented a case of ventricular standstill which had had an arrhythmia similar to that described as a prefibrillatory mechanism. They suggested that the clinical diagnosis of this disturbance is probably impossible without electrocardiographic records.

Most of the patients described by these authors had A-V heart block in some form. The number of such cases which have been described is comparatively small and we feel it worth while to report another case.

CASE REPORT

J. H., a 66-year-old white man, was admitted to the Rhode Island Hospital, May 8, 1945, because of "convulsions." Except for scarlet fever in childhood there was no history of previous illness.

From the Heart Station of the Rhode Island Hospital, Providence, R. I.
Received for publication June 24, 1945.

Two weeks before admission he did not feel well and rested for one day. Three days before admission he developed an illness characterized by chills without cough, which his physician diagnosed as "pneumonia," and for which he was given full doses of sulfadiazine. He progressed favorably and felt well. Four hours before admission he was found on the floor of his bathroom. He was very cyanotic and had generalized twitchings from which he recovered in a short time. Three additional seizures occurred before he reached the hospital.

Soon after admission the patient suddenly became extremely cyanotic, apneic, and pulseless. Oxygen and coramine were administered immediately. Because of the absence of pulse and apical sounds and because of the marked cyanosis, ventricular standstill was considered to be the cause of the syncope. He was given 0.1 Gm. of Metrazol subcutaneously every five minutes, for a total of 0.6 Gm. The blood pressure at this time was not obtainable. The patient gradually lost his cyanosis, became flushed, and then regained his normal color.

Examination between attacks revealed that the patient was a well-developed, rather obese man who was clearly oriented. The blood pressure was 120/90; the rectal temperature, 101.6° F.; respirations, 30; and the pulse rate, 120 per minute. The pulse, initially irregular, gradually became regular. The lungs revealed diminution of breath sounds at the left base and a few crepitant râles. The heart was enlarged to the left and no murmurs were audible. The peripheral vessels were sclerotic.

Electrocardiogram taken at this time (Fig. 1, Column 1) showed a ventricular rate of 80 per minute with a regular sinus rhythm and right bundle branch block.

A few minutes after the tracing was taken the patient suddenly became pale, closed his eyes, and manifested general twitching, following which his eyes opened and he appeared motionless. At this time no pulse or apical heart sound could be heard. His respirations increased to 40. The patient was unconscious and his face was purplish. The inspiratory phase became almost double the expiratory phase and the breathing was noted to be stertorous. He again developed a short convulsive seizure which involved the whole body during which his eyes rolled irregularly to the left and upward. Two minutes later the respirations stopped; he became intensely cyanotic and appeared lifeless. This episode lasted for a period of one minute. Spontaneous revival was associated with the return of the heartbeat and respirations.

Upon regaining full consciousness he was incoherent and confused but within a few minutes became rational and asked, "Did I have another?"

During this period of syncope which lasted about five minutes, he was incontinent of urine.

Within a period of eight hours, the patient had fifteen such attacks, each lasting approximately two to six minutes. An electrocardiogram taken during one of these attacks is shown in Fig. 2. After the fifteenth seizure the patient remained asymptomatic and rested comfortably.

Following his last seizure, the patient was given 0.2 Gm. of quinidine sulfate orally every four hours. This was continued for ten days following which the dosage was gradually reduced to 0.2 Gm. every twelve hours. On the twenty-third day, the drug was discontinued. After he had been free of all symptoms for thirty-seven days, he was discharged from the hospital.

ELECTROCARDIOGRAMS

Fig. 1, Column *2*, shows the electrocardiogram taken May 9, 1945. It shows sinus rhythm, a rate of 76, A-V conduction time of 0.20 second, and right bundle branch block. There is marked slurring of the QRS complexes. The T waves are upright in Leads I and II, slightly inverted in Lead III, and diphasic in CF_4.

A record taken May 11, three days later (Column *3*), shows T-wave changes in all leads. These waves are flattened in Lead I, smaller in Lead II, upright and small in Lead III, and inverted in CF_4. The marked slurring of the QRS complex has disappeared.

A record taken May 15, four days later (Column *4*), shows further changes. These changes suggest that the patient had marked coronary artery disease and that an acute myocardial infarction had initiated his syncopal attacks. Further serial records confirmed this diagnosis.

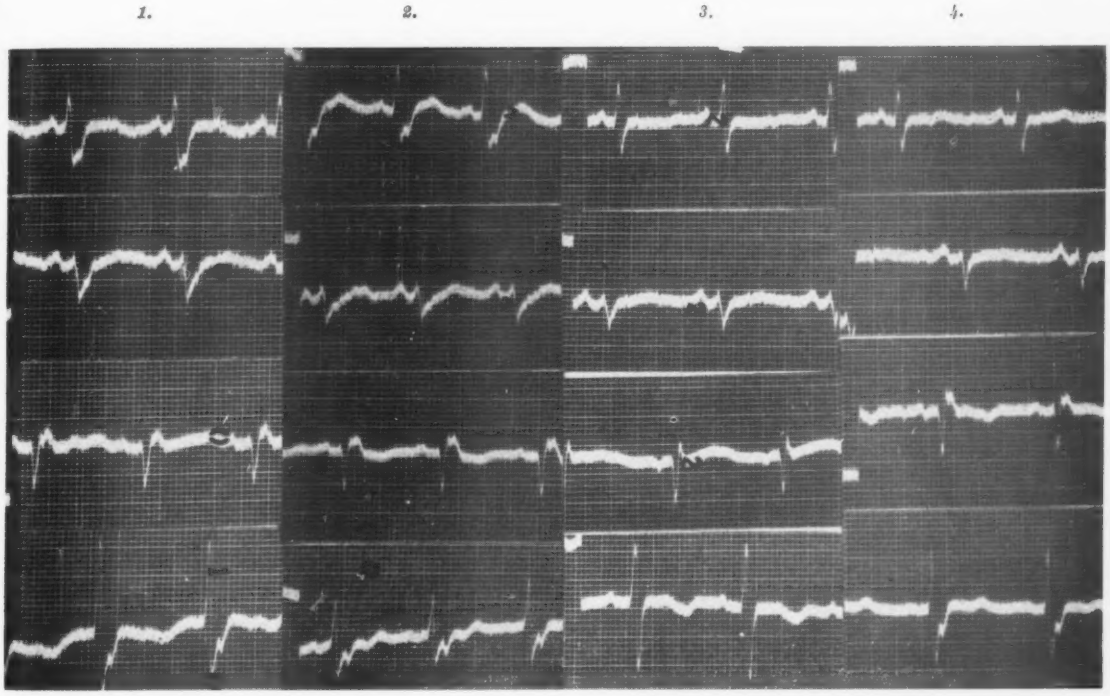

Fig. 1.—Serial electrocardiograms taken on the day of admission between syncopal seizures, on the following day, three days after admission, and seven days after, respectively. They showed normal sinus rhythm, right bundle branch block, and T-wave changes. Further records proved the diagnosis of acute myocardial infarction.

Fig. 2 shows a continuous electrocardiogram (Lead II) taken during and at the end of a typical seizure of transient ventricular fibrillation. The tracing was interrupted only twice, once in the third strip and once in the bottom strip, because the patient had a convulsion and the string could not be controlled. In the second strip the rhythm is quite regular and is similar to the tracing reported by Gertz and his co-workers[8] as representing "ventricular flutter."

Fig. 3 shows a tracing (Lead II) during the same seizure. Strips *1* and *2* show a rapid ventricular rate which varied and oscillations which differ in shape and in amplitude. At this time the patient was extremely cyanotic and pulseless. His eyeballs rolled upward and involuntary urination occurred. The patient was apneic during this period and appeared lifeless. Strip *3* shows a slowing of the ventricular rate to 260 and sudden cessation of the attack with a short postundulatory pause and the establishment of an idioventricular rhythm. With the onset of ventricular contractions, a clonic convulsion threw the string out of the field for a few seconds. As the ventricles commenced to beat the

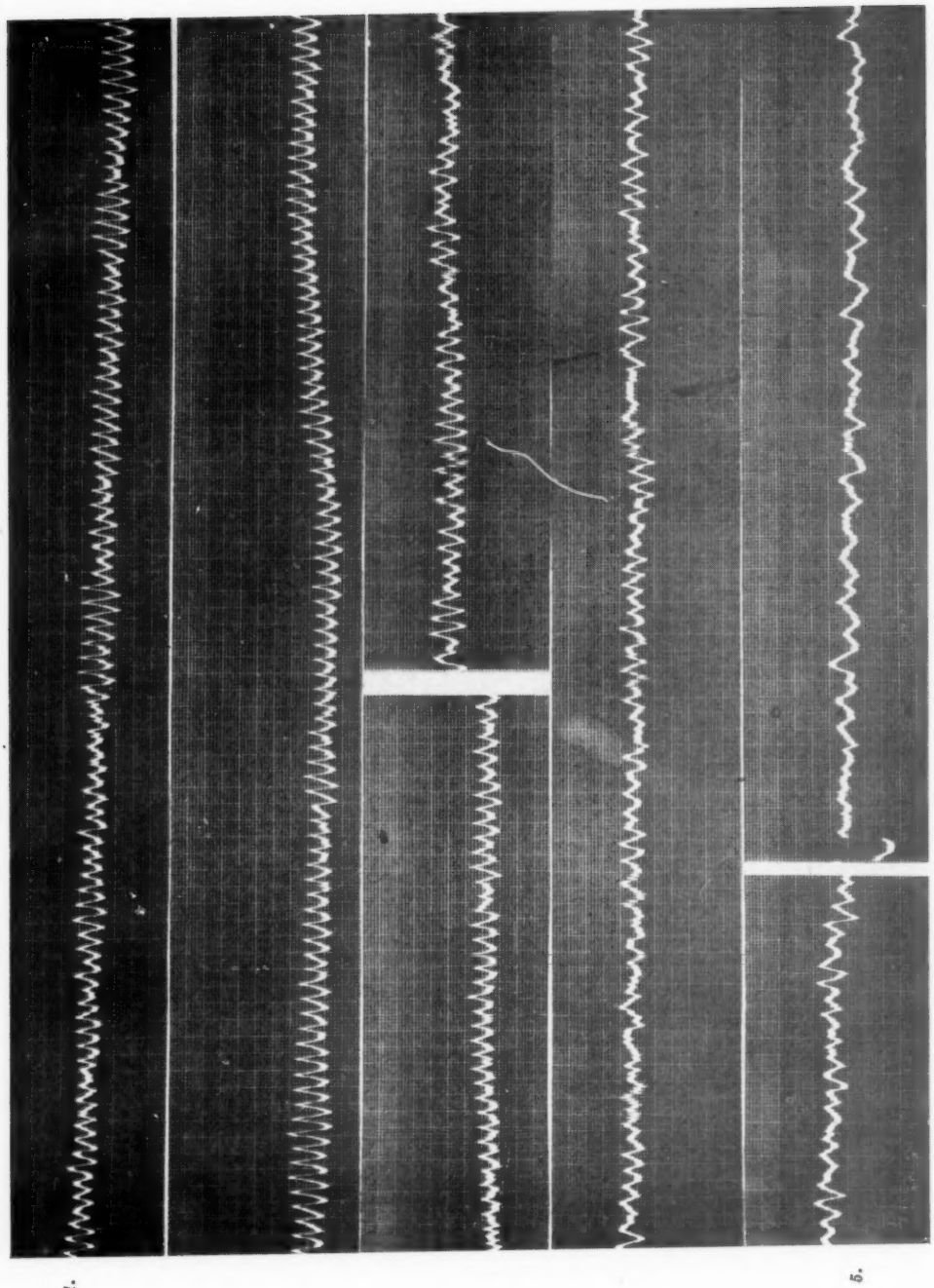

Fig. 2.—A continuous record taken on Lead II, during syncopal attacks showing ventricular fibrillation with waxing and waning of the complexes. The second strip shows a ventricular tachycardia. The record was interrupted only twice, once in the third strip and again in the bottom strip, because the patient had a clonic convulsion and threw the string out of the field.

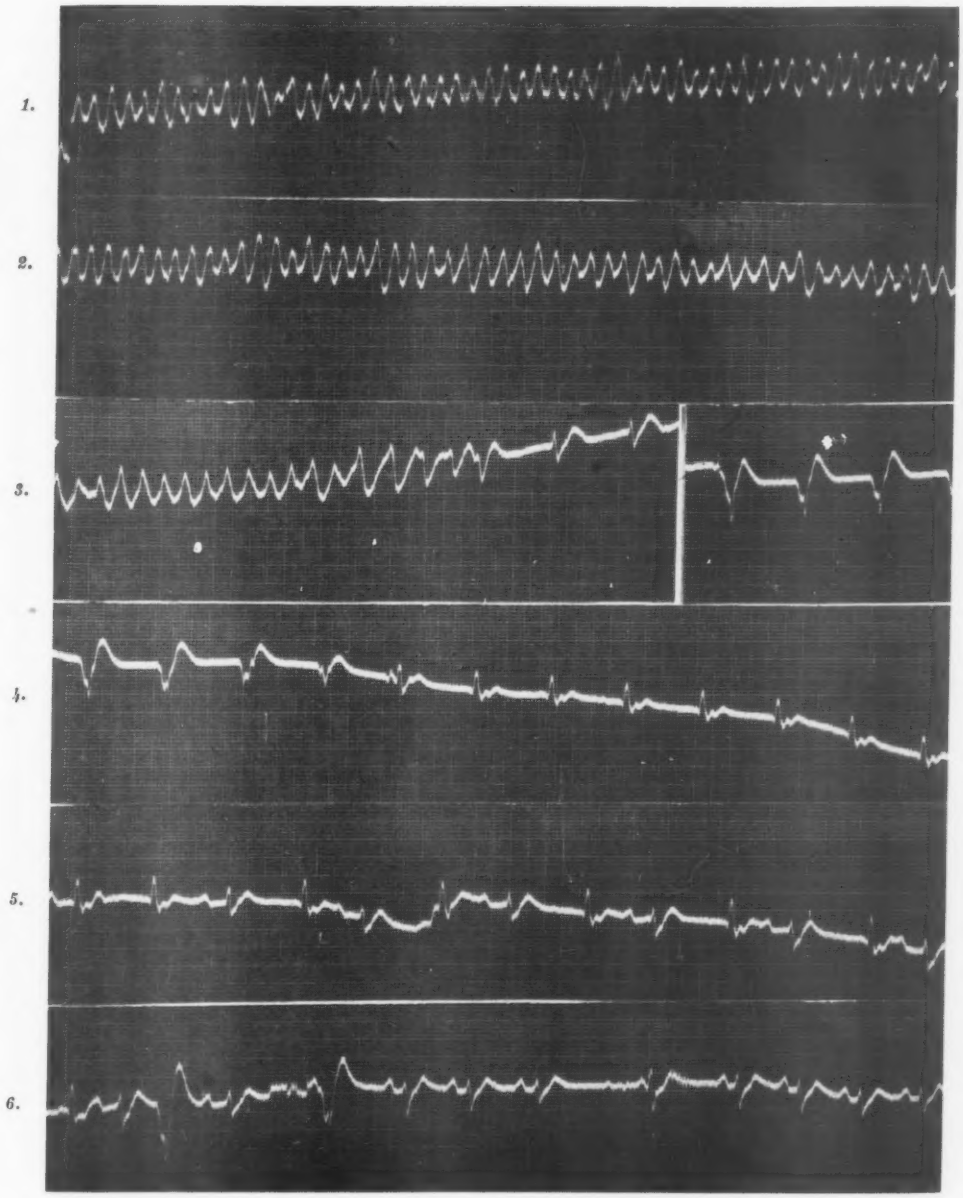

Fig. 3.—A continuous record taken on Lead II showing the end of the syncopal attack. Strip *3* shows the abrupt end of the transient ventricular fibrillation followed by a post-undulatory pause and the onset of an intermediary idioventricular rhythm. In Strip *5* there appear normal complexes in which the P-R interval is increased to 0.30 second. In Strip *6*, following the second ventricular ectopic beat the P-R interval is 0.24 second and at the end of the strip it is 0.20 second.

pulse became perceptible, the cyanosis cleared, and the patient appeared flushed. Gasping respirations began and as the patient regained consciousness he began to breathe regularly. Strip *1* shows idioventricular rhythm. The upright complexes occur regularly and appear to represent an idioventricular rhythm from a different focus. It is possible that these complexes may represent lower nodal rhythm with the P wave following the QRS complex. However, the notching probably is due to slurring of the QRS complex and goes to make up the QRS interval. In the next strip similar complexes appear with occasional ones which resemble the patient's "normal" complexes.

The P-R intervals of these beats are much increased, the duration being 0.30 second. The duration returns to normal in Strip *6* following two ventricular ectopic beats. The P-R interval following the second ventricular ectopic beat in Strip *6* is 0.24 second. Normal rhythm is established at the end of Strip *6*.

DISCUSSION

Most of the cases reported have been associated with some form of heart block or advanced coronary arteriosclerosis. Davis and Sprague[10] observe that the poor prognosis in patients with disease of the bundle tissues suggests that coordinated ventricular action is dependent upon activity of the nodal centers situated in the bundle tissue. It would seem that with complete depression of these tissues, ventricular action, save ventricular tachycardia or ventricular fibrillation, is impossible. This fact, together with the common association of heart block and ventricular fibrillation, they hold as evidence in favor of their hypothesis.

Of interest was the mode of spontaneous recovery of the heart observed in this patient. Schwartz[4] reported two distinct modes of recovery from ventricular fibrillation. In one type, the fibrillation ceased promptly and was followed by a postundulatory pause varying from 0.8 second to 1 second. The basic ventricular rhythm did not appear for several seconds after this, and it was preceded by an idioventricular rhythm. The second type of recovery was also sudden, but was not followed by a postundulatory pause; the idioventricular rhythm arose from the last of the waves terminating the ventricular fibrillation. Fig. 3, Strip *3*, shows the cessation of the ventricular fibrillation followed by a postundulatory pause and the resumption of an idioventricular rhythm.

Davis and Sprague[10] discuss the mechanism of the cessation of attacks in their case. They say, "It is apparent that the depression of the bundle tissues and Purkinje system that we hold responsible for the onset of fibrillation, recovered sufficiently to permit transmission. If this recovery took place in the presence of circus movements in the ventricular muscle, these circus movements would theoretically be brought to a close by the first excitation arising from the node and distributing through the Purkinje system to the musculature. This would destroy any responsive gap and result in a general state of refractoriness from which the ventricle would recover and permit the continuity of rhythmic control from the nodal center. As long as the nodal center and Purkinje fibers

remained excitable, this rhythm would continue. With the appearance of further depression, fibrillation might be precipitated again."

Metrazol was given to this patient at first because it was thought that the syncopal attacks were due to ventricular standstill. This therapy has been suggested by Lueth.[11] When the nature of the disturbance was observed in the electrocardiogram, this drug was discontinued and quinidine sulfate was started by oral dosage.

Levine[12] reported the effect of quinidine in inhibiting ventricular fibrillation. Dock[9] reported a case of recurrent attacks of syncope occurring over a period of eighteen months due presumably to ventricular fibrillation. Subsequent quinidine medication prevented these attacks. Gertz and his co-workers[8] reported a case in which the patient had about twenty syncopal attacks. Quinidine sulfate was ineffective by mouth because of nausea and vomiting. After her last attack the patient lapsed into coma and intravenous quinidine sulfate and other measures were without avail. Davis and Sprague,[10] in their paper, discuss the possible action of quinidine in initiating ventricular fibrillation.

We feel sure that the attacks which are described in this paper stopped spontaneously and not as a result of the quinidine therapy. However the quinidine sulfate was continued for several weeks. Since his discharge the patient has been followed in the Outpatient Department and has remained free of all symptoms.

SUMMARY

1. A patient with coronary artery disease and intraventricular block who suffered from fifteen seizures of unconsciousness during a period of eight hours with spontaneous recovery is reported.

2. The syncopal attacks were shown to be the result of transient ventricular fibrillation.

3. Spontaneous revival from a seizure of ventricular fibrillation was ushered in by the appearance in the electrocardiogram, of a postundulatory pause followed by idioventricular rhythm, and ventricular ectopic beats and finally by normal sinus rhythm.

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Abstracts and Reviews

Selected Abstracts

Allen, Arthur W.: Thrombosis and Embolism. Bull. New York Acad. Med. 22: 169 (April) 1946.

Considering the results of ligation of the femoral veins in 816 patients, Allen believes that thrombectomy and bilateral superficial femoral vein interruption is a safe and satisfactory method of treating early thrombophlebitis. It is a reliable method of preventing pulmonary embolism after clinical chart, signs, or symptoms, show evidence of phlebothrombosis. Prophylactic bilateral superficial femoral vein interruption is a safe and harmless procedure and prevents postoperative thrombosis and embolism. It is particularly suitable in the older age group of patients. Common femoral vein interruption is not recommended in spite of one fatal embolus, occurring in the author's series, from the profunda femoris vein after superficial femoral interruption. Serious sequelae can occur under certain circumstances from common femoral vein occlusion. The technical difficulties far outweigh any added protection to the patient. Dicoumarol in small doses appears to be safe and effective in selected patients as a preventive against thrombosis and embolism. It is useful in conjunction with femoral vein interruption after thrombosis occurs. Careful laboratory observations on the plasma prothrombin time preoperatively and after dicoumarol administration are imperative for the safety of the patient when this drug is used. NAIDE.

Samuels, S. S.: Peripheral Arterial Diseases. Post-Grad. M. J. 22: 22 (Jan.) 1946.

This is a review of some of the diagnostic and therapeutic procedures used in arteriosclerosis and thromboangiitis obliterans. The method of management of gangrene in these two diseases is described in detail. The indications and level of amputation are discussed. NAIDE.

Garber, N.: The Cure of Varicose Veins. South African M. J. 20: 67 (Feb. 9) 1946.

The local and general disturbances incident to the injection of sclerosing solutions with varicosity of the long and short saphenous veins are reviewed. The high percentage of recurrence and dangers attending ligation with retrograde instillation of sclerosing media are pointed out. The author has done 384 multiple resection operations with minor postoperative disability, no recurrence, and no mortality even in the aged. The operation lasts from one and one-half to four and one-half hours in each leg depending upon the size, number, and accessibility of the veins (presence or absence of obesity) and whether the vessels are intimately adherent to the overlying skin as a result of mild but persistent chronic cellulitis. From fifteen to thirty divisions are made under local anesthesia. The incisions lie across the course of the long saphenous and are from ⅛ to 5/16 inch in length. Despite the lengthy course of the operative procedure, shock is absent. Most patients are back at work within three weeks if both legs have been subjected to operation. The operation is recommended by the author as the method of choice for permanent obliteration of varicosities. NAIDE.

Gold, H., Otto, H. L., Modell, W., and Halpern, S. L.: Behavior of Synthetic Esters of Strophanthidin, the Acetate, Propionate, Butyrate, and Benzoate, in Man. J. Pharmacol. & Exper. Therap. **86**: 301, 1946.

Patients with auricular fibrillation were studied to test the effects of the acetate, propionate, butyrate, and benzoate esters of strophanthidin. The heart rates were counted at the apex before and after the oral and intravenous administration of the drugs. All were fully effective in about thirty minutes or less when given intravenously as judged by the decline in heart rate. The oral administration of six times the effective intravenous dose of the acetate ester was not productive of a significant decline in heart rate. The benzoate was most effective by mouth in that only two and one-half times the intravenous dose was required to obtain a reduction in heart rate equivalent to that observed following its intravenous administration. Its full effect was observed in about two to three hours, and its duration of action was nearly eight hours. Orally, the propionate and butyrate esters were intermediate in their efficacy. Toxic effects were observed with all preparations and were the same as with digitalis. FRIEDLAND.

Adlercrantz, E.: On the Neurocirculatory Syndrome (Neurocirculatory Asthenia) in Soldiers. Acta. med. Scandinav. **123**: 219, 1946.

Sixty-eight Finnish soldiers with neurocirculatory asthenia were observed. The majority were between 20 to 29 years of age. Sixty-one were from the laboring group in contradistinction to Lewis's observation in World War I, namely that the majority of his patients left sedentary occupations to enter the army. The most frequent symptoms were previous "heart trouble," dizziness, and headache. Sweats, tremor, tachycardia, and cyanosis of the hands and feet were common. Cardiac hypertrophy as judged by x-ray examinations was present in seven patients. Only occasional patients had systolic murmurs or extrasystoles. The resting systolic pressure was 145 mm. Hg or more in 54 patients, whereas the diastolic pressure was 90 mm. Hg or less in 44 patients. Orthostatic tachycardia and hypotension were observed in 26. The electrocardiogram disclosed left ventricular preponderance in five patients and right ventricular preponderance in nine. Three patients had low or flat T waves in Leads I, II, and III which became higher or upright after exercise. FRIEDLAND.

Teilum, G.: Pathogenetic Studies on Lupus Erythematosus Disseminatus and Related Diseases. Acta. med. Scandinav. **123**: 126, 1946.

A pathologic study of two patients with arteriolitis granulomatosa allergica is presented and certain features common to this disease and to lupus erythematosus disseminatus, rheumatic fever, and periarteritis nodosa are pointed out. It is suggested that although the etiological agents responsible for these diseases may differ, their pathology is indicative of a common pathogenesis. A state of allergy is assumed to constitute the basis for the similarities in tissue changes, the ultimate histopathology being related to the etiological agent and the intensity and extent of tissue reaction induced by the agent. FRIEDLAND.

Apperly, F. L., and Cary, M. K.: The Relation of Arterial Pulse Pressure to Arteriovenous Oxygen Difference, Especially in Arterial Hypertension. Am. J. M. Sc. **211**: 467, 1946.

In a previous paper the authors showed that the arteriovenous oxygen difference in an extremity bears a reciprocal relationship to the product of the pulse pressure times the pulse rate. In this paper, the authors show that hypertensive patients as a group tend to have higher arterial pulse pressures and lower arteriovenous oxygen differences in an extremity. Assuming that the cardiac output in a hypertensive patient differs little from that of the normal individual, the data would indicate that the blood flow to an extremity is greater in the hypertensive patient than in the normal, and that there is, therefore, a greater proportion of blood flow to muscular areas than to the viscera in hypertensive patients. FRIEDLAND.

Straus, R., Dominguez, R., and Merliss, R.: Slowly Progressive Occlusive Thrombosis of the Abdominal Portion of the Aorta. Am. J. M. Sc. 211: 421 (April) 1946.

Three cases of slowly progressive occlusive thrombosis of the abdominal portion of the aorta are presented. The disease is usually secondary to a severe ulcerative arteriosclerosis of the arterial wall, but may follow an embolism to the bifurcation of the aorta, or more rarely, thrombosis of the pelvic arteries after irradiation. Its mean autopsy incidence is 0.12 per cent. The characteristics of this syndrome that permit differentiation from other forms of aortic occlusion are: insidious onset; protracted course; usually, but not always, absence of gangrene; absence of pulses in both lower extremities; intermittent claudication; and the appearance of arterial hypertension or of signs of visceral infarction years after the onset of claudication in the legs. NAIDE.

Ranström, S.: Amyloidosis Myocardii. Acta. med. Scandinav. 123: 111 (No. 2) 1946.

Three cases of "primary" cardiac amyloidosis are reported and the thirty cases in the literature are reviewed. The only fairly constant clinical findings were rapid sedimentation rates, thought to be the result of hyperglobulinemia; and a slight or moderate hypotension. Low voltage in the electrocardiogram and signs of myocardial insufficiency sometimes occurred. The heart was frequently enlarged, but its gross appearance in one of the author's cases was normal except for hypertrophy. Usually there was a greenish yellow coloration and a semiopaque sheen when involvement of the myocardium was severe and diffuse. Microscopically there might be diffuse or spotty interstitial deposits, though amyloid was never found actually within the muscle fibers themselves. Subepicardial, subendocardial, and valvular deposition was sometimes seen, the mitral valve was involved in one of the author's cases. Another type of deposition was amyloidosis of the smaller coronary artery branches, in which the media and intima were almost entirely replaced by amyloid and surrounded by a relatively normal adventitia. No definite cause for the amyloid was found in any of the three cases reported by the author. SAYEN.

Gladnikoff, H.: The Roentgenological Picture of the Coarctation of the Aorta and Its Anatomical Basis. Acta. radiol. 27: 8 (No. 1) 1946.

The author correlates the roentgenologic picture with the operative findings in three cases of coarctation of the aorta which were repaired by Crafoord. He emphasizes that the leftward convexity in the upper mediastinum was the dilated left subclavian artery although it had sometimes been mistaken for the aortic knob. In all three cases the coarcted area lay at the angle of juncture of the subclavian artery and the aortic arch or 3 to 5 cm. below it, but was drawn within the mediastinal shadow. Below the depression in the left mediastinal border the thoracic aorta could be seen, although not clearly. The aortic knob in the anteroposterior and the arch in the left anterior oblique views were poorly seen in spite of hypertension which was expected to increase visibility. This was explained by the shortening effects of low pressure in the aorta below the coarctation, by contraction of the adjacent aortic wall, and by the fact that the aorta was pulled inward, downward, and posteriorly by the shortening of the ductus botalli. The poor roentgenologic visualization is believed to be due to the effect of coarctation on aortic length and position. Hence, the disappearance of the shadow of the aortic arch in the x-ray is by no means pathognomic of coarctation and can occur in any condition that causes shortening of the aorta, such as congenital hypoplasia. SAYEN.

Savilahti, M.: On the Normal and Pathological PQ Time of the Electrocardiogram. Acta. med. Scandinav. 123: 252 (No. 3) 1946.

From statistics based on 872 cases of all ages the author concludes that the length of the P-Q interval is not directly related to the heart rate and that it remains very constant in any particular healthy individual except for a gradual increase with age in childhood

and adolescence. The upper limits of normal for the younger age groups in the series were 0.15 second below the age of 5 years, 0.17 second between 5 and 10 years, and 0.20 second after the age of 15 years. In fever, the standing posture, and after exercise, the P-Q interval often shortened; but this was not proportionate to the increased heart rate in such states and not infrequently occurred when the rate remained relatively constant.

SAYEN.

Bang, J.: A Peculiar Conduction Disturbance Persisting Latently After Recovery From Complete Heart Block and Disclosed Only by Electrocardiography Following Exercise. Acta. med. Scandinav. 123: 551 (No. 6) 1946.

The author reports the case of a 15-year-old boy who developed complete heart block three weeks after a streptococcal tonsillitis and was subject to attacks of syncope associated with complete pallor and mild spasms. The heart rate during block was 40 per minute; the blood pressure was 90/80, and the sedimentation rate was 56 mm. per hour. Leucocytosis was present and antistreptolysin titers were significantly elevated. Recovery was gradual; a two-to-one heart block was present on the seventh day, and partial block was recorded on the ninth day after onset. The P-R interval was markedly prolonged for thirteen days, and on discharge from the hospital it was still as high as 0.22 second.

The patient was re-examined one year later and the abnormal P-R interval, which was still present, was the only significant finding. After violent exercise, a marked arrhythmia occurred, consisting of short runs of six or seven rapid beats, and a steadily increasing P-R interval which reached 0.30 second, after which there was a slight pause, which may have represented a dropped beat, and the rate decreased sharply. The next several beats were at a slow tempo with a P-R interval of 0.17 second. This cycle was repeated several times, and, after a lapse of about twenty minutes, although the rate was regular, the P-R interval was noted to be 0.30 second, diminishing only gradually to 0.23 second. Re-examination the following year showed the identical picture, although the patient felt quite well and led an active life throughout the period of examination and the intervals between.

SAYEN.

Magnasson, P.: Auricular Standstill. Acta med. Scandinav. 123: 519 (No. 6) 1946.

Three new cases are added to the thirty-one collected from the literature. The criteria were a regular ventricular rate and no auricular deflections in any limb or precordial lead. The commonest causes of the disorder appeared to be digitalis or quinidine toxicity. The authors emphasize the necessity of frequent electrocardiograms in patients who are receiving large doses of digitalis with normal rhythm or patients with auricular fibrillation who regain normal rhythm, since there are no diagnostic clinical symptoms of auricular standstill and since in animals this condition is frequently a precursor of ventricular standstill.

SAYEN.

Lindqvist, T., and Söderström, N.: An Unusual Electrocardiographic Manifestation of Intra-Auricular Dissociation in a Pair of Identical Twins. Acta med. Scandinav. 123: (No. 1) 1946.

Electrocardiographic studies were made in a pair of 42-year-old identical twins with absolute arrhythmias. They were found to have a totally irregular ventricular rate but with P waves preceding all complexes. The P-R intervals varied from 0.23 to 0.5 second. Rare periods of complete atrioventricular dissociation occurred. Most of the P waves in limb leads were double, the two peaks separated by 0.08 to 0.1 second. The second (usually inverted) component of these P waves was simultaneous with the intrinsic auricular deflection in esophageal leads, while the first component was largest in a precordial lead near the sternum in the third right intercostal space. They were thought to be, respectively, left and right auricular in origin and their separateness was attributed to delayed inter-

auricular conduction. With increased heart rates small irregular *f* waves appeared in one case, in addition to the double P waves. Administration of ½ mg. of atropine sulfate caused the base line to show coarse flutterlike waves, every other one being accompanied by a P wave. The authors believe that the bizarre mechanism was caused by a localized area of constant fibrillation, probably in the right auricle, surrounded by a ring of refractory muscle transmitting a limited number of impulses to which the remaining muscle of the right and left auricles responded usually, and the ventricles always, with a totally irregular rhythm. SAYEN.

Lequieme, J., and Denolin, H.: Circulatory Changes Following the Injection of Hypertonic Saline Solutions. Application to the Study of Angina Pectoris. Arch. d. mal. du cœur. 38: 231 (Sept.-Oct.) 1945.

Observations were made on the effect of intravenous injections of hypertonic saline solution in patients who had coronary disease. Forty patients were studied, all of whom presented a typical history of angina of effort. The technique involved recording the electrocardiogram from the limb leads before, immediately after, and five minutes after the rapid intravenous injection of 40 c.c. of 20 per cent saline solution.

The procedure was well tolerated. All patients noted a sensation of warmth resulting from the injection. Six patients had anginal pain and, in two instances, the pain was severe. In 38 of the 40 patients, the heart rate was accelerated. In 14 patients, the electrocardiogram showed transient S-T interval deviation which was most conspicuous in Leads II and III. In 12 patients, the T waves became flattened in Leads I and II. In 14 patients, the injection produced no significant change in the electrocardiogram. It is noteworthy that in the latter group, most of the patients had abnormal electrocardiograms before the test.

In normal subjects and in cardiac patients without coronary disease, the injection produced tachycardia and occasionally some flattening of the T waves, but there have been no instances of S-T interval deviation. The effect of intravenous hypertonic saline on the electrocardiogram of patients who have coronary disease is attributed to the resultant increase in work of the heart. The procedure is recommended as a substitute for the exercise test in the diagnosis of angina pectoris. LAPLACE.

Gillman, T., and Gillman, J.: The Value of Speransky's Method of Spinal Pumping in the Treatment of Rheumatic Fever and Rheumatoid Arthritis. Am. J. M. Sc. 211: 448 (April) 1946.

The method of spinal pumping first described by Speransky, in 1935, was utilized by these authors in the treatment of 70 patients suffering from acute, subacute, or chronic forms of rheumatism with joint involvement. All the patients, with three exceptions, were adults. In all but two instances, 10 Gm. of sodium salicylate in divided doses were administered orally or rectally twenty-four hours before pumping and for twenty-four to forty-eight hours after pumping. The actual "pumping" consists of withdrawal into the barrel of a 10 c.c. syringe of cerebrospinal fluid, and then re-introducing the fluid into the subdural space. This procedure is performed with the patient in the left or right lateral position. In most of the cases in this series, 10 c.c. of cerebrospinal fluid (only 6 c.c. in children) were withdrawn and re-introduced twenty times. At the completion of the spinal pumping, 10 c.c. of the spinal fluid were removed and discarded. This procedure usually takes forty or fifty minutes.

Of 48 cases of acute or subacute arthritis, 42 showed objective evidence of improvement. The majority of the patients (70 per cent) were relieved within twelve to thirty-six hours, and another 20 per cent responded at the end of seventy-two hours. The remaining cases showed a steady improvement which was maximum at the end of two to three weeks. No recoveries among chronic cases were observed but 12 of the 22 cases were considerably relieved.

In general, the results obtained confirm those recorded by Speranksy. It is the opinion of the authors, in agreement with Speransky and others, that the nervous system plays a considerable role in the pathogenesis of rheumatic fever, rheumatoid arthritis, and other inflammatory processes, and that spinal pumping produces some interference with the nervous mechanism which leads to favorable responses in the various forms of rheumatism resistant to the usual forms of therapy. BELLET.

Kittredge, W. E., and Brown, H. G.: The Present Status of Unilateral Renal Hypertension. J. Urol. **55:** 213 (March) 1946.

The present status of unilateral kidney pathology in producing hypertension is considered, with particular reference to the indications for nephrectomy of the diseased kidney. This procedure has been performed in every type of surgical kidney in recent years with the hope of relieving hypertension.

Numerous clinical investigators have pointed out that the influence of hypertension in a series of patients with unilateral kidney disease is actually no greater than the incidence in any group of patients of comparable age chosen at random. From a study of conflicting observations and careful follow-up of patients, the authors have reached the following conclusions: no permanent change in blood pressure can be reasonably expected to follow removal of a functionless kidney, whether the diseased kidney was the original cause of the hypertension or not; the renal lesion associated with hypertension which was most amenable to surgical treatment was atrophic pyelonephritis; and the next most common lesion associated with hypertension was renal neoplasm, followed by renal lithiasis, hydronephrosis, tuberculosis, and polycystic kidneys.

Although hypertension associated with surgical lesions was often relieved by nephrectomy, the blood pressure often also returns to normal following nephrolithotomy and renal drainage. This reduction in blood pressure may persist for a year or more after operation and then return to its previous level. This may be explained on the grounds that a toxic or irritant lesion has been eliminated and that, when this influence has worn off, the underlying essential hypertension reasserts itself. BELLET.

Mokotoff, R., Brams, W., Katz, L. N., and Howell, K. M.: The Treatment of Bacterial Endocarditis With Penicillin, Results of 17 Consecutive Unselected Cases. Am. J. M. Sc. **211:** 395 (April) 1946.

These authors report a series of 17 consecutive patients with subacute bacterial endocarditis, 14 of whom have fully recovered from their infection. These patients were observed for a period of eight to twenty months following cessation of therapy. The susceptibility of the organism to penicillin is one of the most important factors in determining the outcome of therapy. These authors agree with Loewe that the best results are obtained when penicillin blood serum levels are maintained between five and ten times the "in vitro" sensitivity figure. Since investigation has shown that there is little penicillin remaining in the blood serum sixty to seventy-five minutes after a single intramuscular injection and practically none at the end of two hours, intermittent intramuscular injections were employed every hour on the hour day and night for the entire period of treatment. The usual daily dose was 200,000 to 300,000 units; the more resistant cases received 1 million to 3 million units. The usual course was planned for twenty-one days. It is of some interest that one of their patients, who died because of progressively severe congestive failure (six months after successful penicillin therapy) revealed at autopsy healed subacute bacterial endocarditis of the mitral and aortic valves. BELLET.

Heuper, W. O.: Atheromatosis in Dogs Following Repeated Intravenous Injections of Hydroxycellulose. Arch. Path. **41:** 130 (Feb.) 1946.

Heuper, continuing his studies on the genesis of atheromatosis, recorded the effects of intravenous injections of hydroxycellulose in various concentrations. This was injected daily for periods of six to twelve weeks. The viscosity of the solutions was an important

factor in the production of atheromatosis; the least viscid solution was responsible for the most severe and generalized lesions. Typical foam cells, fibrous cushions, and circumscribed hyaline thickenings of the intima, often associated with degeneration and calcification of the media of the aorta and of the medium-sized branches were noted in the dogs receiving injections of hydroxycellulose of medium and low viscosity. Solutions of heavy viscosity produced no intravascular pathologic changes. On the other hand, the latter injections resulted in leucopenia and anemia. GOULEY.

Koletsky, S.: Gross Vascularity of the Mitral Valve as a Stigma of Rheumatic Heart Disease. Am. J. Path. 22: 351 (March) 1946.

Koletsky studied the vascularity of the mitral valve of 150 hearts with and without gross rheumatic heart disease, all of which showed gross vascularity of the anterior mitral leaflet. The hearts observed were divided into three groups as follows: Group 1 contained 50 hearts with no conclusive gross rheumatic disease, Group 2 included 50 hearts with nondeforming rheumatic mitral disease, and Group 3 included the 50 hearts with mitral stenosis. Fifty nonrheumatic adult hearts with grossly avascular mitral valves were included as a control. It was found that a large percentage of hearts with no gross rheumatic disease which presented gross vascularization of the mitral valve leaflet showed microscopically endocardial reduplications and cellular exudate characteristic of rheumatic valvulitis. Group 2 has the same microscopic stigmata but in a higher percentage. The group of hearts with mitral stenosis showed the highest percentage. The control group showed very little or no vascularity of the anterior mitral leaflet and no microscopic stigmata.

Koletsky concludes that hearts with diffuse gross vascularity of the mitral valve almost uniformly show microscopic stigmata of inflammatory disease of rheumatic origin. The presence of small thick-walled arteries of musculoelastic type in the mitral valve is considered by Koletsky to be characteristic and probably pathognomic of rheumatic fever. GOULEY.

Askey, J. M.: Quinidine in the Treatment of Auricular Fibrillation in Association With Congestive Failure. Ann. Int. Med. 24: 371 (March) 1946.

Quinidine is ordinarily considered to be contraindicated for auricular fibrillation in association with congestive failure, or in association with severe heart disease. In certain instances, however, its use has been lifesaving and in a number of desperately sick patients, it has improved the patient's cardiac status for many months. The real dangers of quinidine are those of embolism, sudden death, and production of ectopic ventricular rhythms. This study concerns itself with a statistical evaluation of the dangers of quinidine, particularly in the presence of congestive heart failure and serious heart disease. This is done in an attempt to determine any deleterious effects in such patients which would outweigh any beneficial action which may be desired. This author found that quinidine is apparently no more dangerous to patients with congestive failure than the natural dangers of the heart condition itself. Among patients with congestive failure who improve adequately with digitalis and rest, along with other measures, quinidine therapy might be tried. The presence of conduction defects appears to be a contraindication to its use. In the absence of such abnormalities there would seem to be no reason why every patient with uncontrolled congestive failure should not be given a chance with quinidine. Even if the ventricular rate is slow, reversion to sinus rhythm may relieve congestive failure. The usually accepted contraindications in the use of quinidine, namely congestive failure, repeated embolism, long standing auricular fibrillation, and conduction defects, are not considered to be absolute contraindications. BELLET.

Fox, M. J., and Bortin, M. M.: Rubella in Pregnancy Causing Malformations in Newborn. J. A. M. A. 130: 568 (March 2) 1946.

Much interest has recently developed concerning the influence of rubella early in pregnancy upon the production of congenital malformations. Some authors have even suggested therapeutic abortion be performed when rubella occurs early in pregnancy. In a

series of eleven cases observed by these authors, only one evidenced a pathologic course. Their records do not justify the conclusions of previous authors concerning the influence of rubella in producing congenital malformation. They suggest that this subject deserves further careful consideration and investigation. BELLET.

Epidemiology Unit No. 82, U. S. Naval Hospital, Treasure Island: Observations on the Treatment of Scarlet Fever With Penicillin. Am. J. M. Sc. 211: 417 (April) 1946.

In view of recent reports showing the efficacy of penicillin therapy in the treatment of streptococcal pharyngitis and scarlet fever, an investigation was made on 118 patients who were members of the Naval personnel. All patients treated with penicillin showed a good clinical response in that the temperature dropped to normal and there was marked symptomatic improvement in twenty-four to forty-eight hours. The incidence of complications was found to be highest (31 per cent) in that group receiving 240,000 units in six days and lowest (6 per cent) in the group receiving 480,000 units in eight days.

The rate of recurrence of positive cultures was also lowest (8 per cent) in the group receiving the higher penicillin dosage. It was therefore concluded that the use of penicillin over an eight-day period is a satisfactory method for the treatment of scarlet fever and for preventing the establishment of a beta hemolytic streptococcus carrier state in the convalescent patients. BELLET.

Hubacker, V. O.: Beitrag zur Beurteilung des runden Überganges von R und die ST Strecke in Electrokardiogramm. Helvet. med. acta, Series A (March) 1946.

1. The hypothesis according to which the rounded transition of the R wave to the S-T interval is of cardiac origin must be definitely abandoned.

2. The rounded transitions occur when polarization is small within the electric circuit patient-electrocardiograph; they disappear and become pointed S waves when polarization within this circuit is considerable.

3. The polarization capacity of the skin is small in the presence of poor blood flow and large when the flow is good.

4. The signs of polarization in the electrocardiogram depend upon the form of the latter (the part above and below the isoelectric line), upon the apparatus (resistance), and upon the functional processes in the skin of the patient (blood flow). AUTHOR.

Davidson, C. S., Lewis, J. H., Tagnon, H. J., Adams, M. A., and Taylor, F. H. L.: Medical Shock: Abnormal Biochemical Changes in Patients With Severe, Acute Medical Illnesses, With and Without Peripheral Vascular Failure. New England J. Med. 234: 279 (Feb. 28) 1946.

This study was undertaken to determine the relationship of peripheral vascular failure, uncomplicated by traumatic conditions, to the biochemical changes which accompany shock in experimental animals and injury in man. Observations were made on a series of twelve patients who were suffering from severe medical illness with or without the presence of peripheral vascular failure. The presence of diabetes mellitus was excluded.

It was found that the biochemical abnormalities which occurred in these patients were similar to those which occur in various traumatic conditions, hemorrhage, and anoxia. They consisted of hyperglycemia, lactacidemia, a fall in the bicarbonate reserve, reduction in oxygen saturation of the peripheral blood, frequent elevation of the alpha amino nitrogen of the blood plasma, and usually a lengthening of the prothrombin time and an elevation of the icterus index. Although the primordial cause is not known, the authors suggest the possibility that tissue anoxia which accompanies peripheral vascular failure, leads to increase in glycogenolysis and possible gluconeogenesis with resultant hyperglycemia. A marked correlation was found between the profoundness of the biochemical abnormality and the degree of the vascular failure. LAPLACE.

Announcements

INTER-AMERICAN CONGRESS OF CARDIOLOGY, MEXICO CITY, OCT. 6-12, 1946

There will be an Inter-American Congress of Cardiology in Mexico City, Oct. 6-12, 1946. The meetings will be held in the Institute of Cardiology. This Congress is being sponsored by the Inter-American Society of Cardiology and the National Societies of Cardiology of the Continent. Prominent European cardiologists have been invited to attend. The American Heart Association has been designated as the representative of this Congress in the United States, and all applications to participate in the scientific meetings or to attend as guests should be addressed to this Association, 1790 Broadway, New York 19, New York.

FELLOWSHIPS AVAILABLE FOR THE STUDY OF RHEUMATIC FEVER

The American Council on Rheumatic Fever of the American Heart Association announces that it will entertain applications for American Legion fellowships for the study of rheumatic fever. Applications will be accepted from recognized institutions concerned with the study of rheumatic fever and rheumatic heart disease. Two fellowships are available. Each is for a period of three years and carries a stipend of $3,500, $4,000, and $5,000 for the first, second, and third years, respectively.

Each application should supply information concerning the institution, the projected study, and the individual proposed for the fellowship. Applications will be received until Aug. 1, 1946, and will become effective Sept. 1, 1946.

The American Legion fellowships for the study of rheumatic fever have been made available by a grant from the American Legion and the Women's Auxiliary of the American Legion as part of their program of fostering research in rheumatic fever and rheumatic heart disease through the American Council on Rheumatic Fever of the American Heart Association.

Errata

Mainly because of distance and the difficulty of rapid mail communication, there were several errors in the paper by Dr. R. H. Goetz of Cape Town, South Africa, on "The Rate and Control of the Blood Flow Through the Skin of the Lower Extremities," which appeared in the February, 1946, issue of the JOURNAL, Volume 31. We regret exceedingly that these errors were made. We are glad to publish the following corrections so that the author's intended meaning will be clear.

1. Page 154, the second line of the last paragraph should read "multiple pinpricks" and *not* "multiple principles."

2. Page 164, five lines from the top of the page, should read: "Fig. 14 shows one of the arteries of the digit tested" and *not* "Fig. 14 shows the results of testing one of the arteries of the digit."

3. Page 172, the sixth line of the second paragraph should read: "This decrease in blood flow following body heating has been explained as follows: Since body heating causes a release of the vasomotor tone in the normally innervated extremities, it follows . . . to the unsympathectomized one."

4. Page 177, the last sentence in the first paragraph under Discussion should read: "Failure of the pulse has *therefore* to be accounted for" *not* "Failure . . . has *yet* to be . . ."

5. Page 177, the first line of the last paragraph should read: "The possibility of such a wide range in blood flow, under the control of the autonomic nervous system, is part of the body's mechanism for temperature regulation." *Not* "The possibility exists . . ."

American Heart Association, Inc.

1790 Broadway at 58th Street, New York, N. Y.

THE American Heart Association is the only national organization devoted to educational work relating to diseases of the heart. Its activities are under the control and guidance of a Board of Directors composed of thirty-three eminent physicians who represent every portion of the country.

A central office is maintained for the coordination and distribution of important information. From it there issues a steady stream of books, pamphlets, charts, films, lantern slides, and similar educational material concerned with the recognition, prevention, or treatment of diseases of the heart, which are now the leading cause of death in the United States. The American Heart Journal is under the editorial supervision of the Association.

The Section for the Study of the Peripheral Circulation was organized in 1935 for the purpose of stimulating interest in investigation of all types of diseases of the blood and lymph vessels and of problems concerning the circulation of blood and lymph. Any physician or investigator may become a member of the section after election to the American Heart Association and payment of dues to that organization.

The income from membership and donations provides the sole financial support of the Association. Lack of adequate funds seriously hampers more intensive educational activity and the support of important investigative work.

Annual membership is $5.00. Journal membership at $11.00 includes a year's subscription to the American Heart Journal (January-December) and annual membership in the Association. The Journal alone is $10.00 per year.

The Association earnestly solicits your support and suggestions for its work. Membership application blanks will be sent on request. Donations will be gratefully received and promptly acknowledged.